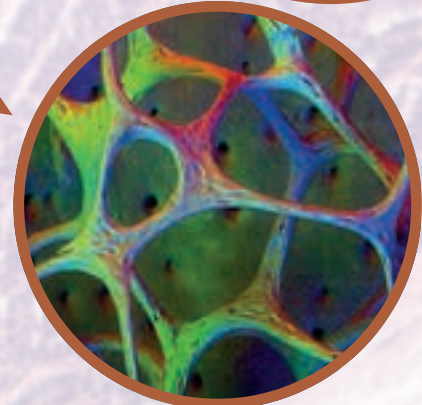
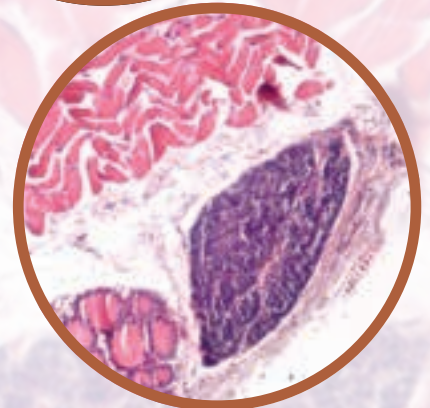
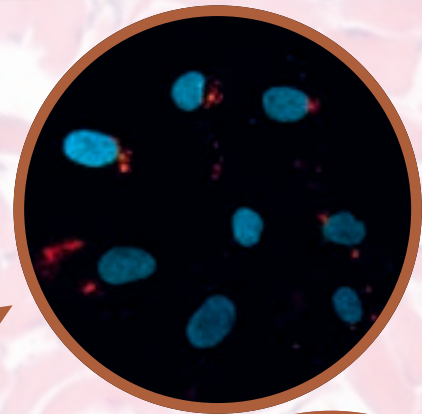
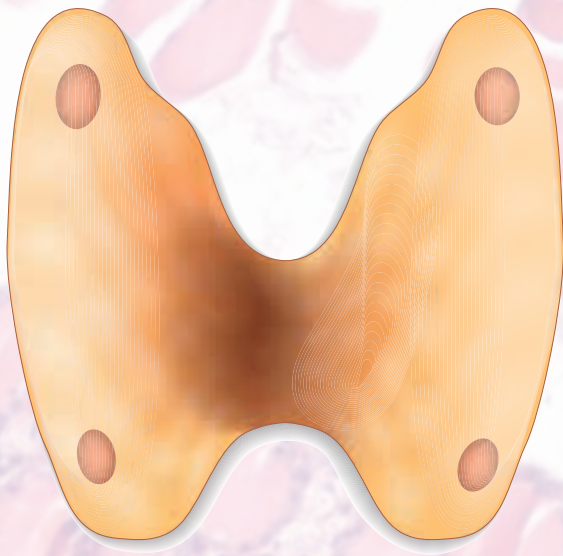


THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

The parathyroids **FROM CELL TO SKELETON**



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A word from THE EDITOR...



A year. A year that has felt like 5 years. In February 2020 I was in Johannesburg, watching the teenager play cricket and discovering a different city. Later, as the storm clouds gathered, I wondered if I should fly him home early, so he would be safe. Who knew then that the UK would have one of the highest death rates in the world from this pandemic?

Now I am working in a nursing role in ICU: double-pumping noradrenaline, suctioning coronavirus out of lungs. Bowie said 'tomorrow belongs to those who can hear it coming'. I couldn't hear it coming until this week when all of a sudden, a mixture of government announcements and a date for my second dose of vaccine meant I almost feel hopeful. Until now I've felt like I've been living in a suspended reality where tomorrow is the same as today. Life consists of 12-hour shifts in the hospital and remote clinics at home, vaccinating for light relief. I'm still waiting for these times to pass because what I really, really want to do is to have some fun. I'll have to wait a little longer and, in the meantime, be thankful that my family and friends are all just about OK.

This issue of *The Endocrinologist* focuses on the parathyroids. We are extra grateful to all the contributors, writing for us in the midst of the turmoil. We have articles ranging from organising services to deliver care during a pandemic, by Neil Gittoes and colleagues (page 6), to novel treatment for hypoparathyroidism with recombinant parathyroid hormone, by Jeremy Turner and colleagues (page 10). Key to medicine is listening to our patients, and Liz Glenister describes living with hypoparathyroidism on page 16.

To mark International Women's Day, we share an article from the archives on page 30; a conversation between Phillipa Saunders and Kerri Devine, on the challenges of networking, peer support, balancing family, budgeting time, and having a career.

Something I have found joyful during this pandemic are SIMBA and CoMICs, educational materials that are the brainchildren of Punith Kempegowda. On pages 20–22, he and his teams describe their work. I am also hoping he shares with me the secret to his seemingly endless energy.

So maybe there is hope and soon we can have some fun, and see and hug our families and friends. I hope this is an enjoyable read and that you can forget about COVID for a short while, at least. And, if not, there is always Bowie to listen to...

HELEN SIMPSON

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www.endocrinology.org/endocrinologist

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Editor:
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Managing Editor: **Jane Shepley**
Sub-editor: **Caroline Brewer**
Design: **Ian Atherton, Corbicula Design**

Society for Endocrinology
Starling House
1600 Bristol Parkway North
Bristol BS34 8YU, UK
Tel: **01454 642200**
Email: members@endocrinology.org
Web: www.endocrinology.org
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The Society welcomes news items, contributions, article suggestions and letters to the Editor. We would also like to hear your feedback on this issue of the magazine.

Deadline for news items for the SUMMER 2021 issue: **4 April 2021.**

Cover: ©Kate Lines, Mark Stevenson, Kreepa Kooblall, Shutterstock
(more info about the cover image on page 4)



Mark Gurnell



Barbara McGowan

SOCIETY UPDATE

The Society welcomes Professor Mark Gurnell (Cambridge) as your new Treasurer. We send our grateful thanks to Dr Barbara McGowan, who completed her term of office at the end of 2020.

SHARE YOUR WORK WITH THE ENDOCRINE COMMUNITY

You can apply now for our Early Career Prize Lectures, which include the opportunity to present at SfE BES 2021, receive an honorarium and write an article for *The Endocrinologist*! The deadline is **30 April 2021**; see www.endocrinology.org/grants-and-awards.



Inês Cebola, 2019 Science Prize Lecturer

NURTURING EMERGING TALENT: LEADERSHIP AND DEVELOPMENT AWARDS

Applications will be open for the Society's Leadership and Development Awards from 1 April until 14 May 2021. This programme aims to advance and support the future leaders of our discipline and provides a wide range of opportunities for early career members. Find out more at www.endocrinology.org/leadership.



SOCIETY DISCOUNTS FOR BNA2021 REGISTRATION

Your Society is a partner organisation for the BNA2021 Festival of Neuroscience on 12–15 April 2021. This British Neuroscience Association online event includes our convened and supported session 'Brain energy sensing, adaptations and alterations to network outputs'. Go to the Members' Area to get your discount code for reduced fees. Find out more at <https://meetings.bna.org.uk/bna2021>.

HAVE YOUR SAY AND MAKE A DIFFERENCE

Who should be the Society's next President-elect? Nominate your selection for the vacancy on Council before **17 September 2021**.

A wide range of members from all career levels, backgrounds, areas of expertise and locations are also needed to bring fresh perspectives and new ideas to our Committees for 2022. If you would like to represent the Society's members, look at the Committee remits and nominate or apply by **1 October 2021**.

Further information on Council and the Committees can be found at www.endocrinology.org/about-us/governance along with nomination and application details.

BRING ENDOCRINOLOGY TO LIFE ON VIDEO

Our Student Video Award is back! Are you, or do you know, a student with a passion for endocrinology? Producing a short video on 'hormones in the news' will help students develop their science communication skills and boost their CVs. The award is now open to both undergraduate and postgraduate students. The application deadline is **30 April 2021**; find out more at www.endocrinology.org/video.



2020's winning video by Aqua Asif

SOCIETY CALENDAR

17 September 2021
COUNCIL NOMINATION DEADLINE

1 October 2021
COMMITTEE APPLICATION DEADLINE

8–10 November 2021
SfE BES 2021
Edinburgh, UK

www.endocrinology.org/events for full details

SOCIETY-ENDORSED EVENTS

12–15 April 2021
BNA2021 FESTIVAL OF NEUROSCIENCE
Online

4 May 2021
RSM CLINICAL UPDATE: GENETICS AND ENDOCRINOLOGY (PT 1)
Online

GRANT AND PRIZE DEADLINES

10 March 2021
TRAVEL GRANTS

17 March 2021
SUMMER STUDENTSHIPS

24 March 2021
PUBLIC ENGAGEMENT GRANTS

1 April –14 May 2021
LEADERSHIP AND DEVELOPMENT AWARDS

7 April 2021
PRACTICAL SKILLS GRANTS

30 April 2021
EARLY CAREER PRIZE LECTURES

30 April 2021
STUDENT VIDEO AWARD

5 May 2021
EARLY CAREER GRANTS

5 May 2021
EQUIPMENT GRANTS

5 May 2021
ENDOCRINE NURSE GRANTS

26 May 2021
MEETING SUPPORT GRANTS

www.endocrinology.org/grants for full details of all Society grants and prizes

ONLINE TRAINING OPPORTUNITIES

After the successful introduction of our online webinar series in 2020, the Society has devised the SfE Skills Academy for 2021, to help support your learning and professional development during the continuing constraints of COVID-19 lockdown. You can find out more on page 19 or at www.endocrinology.org/events.



RESEARCH SKILLS WEBINAR

Ensuring your research is statistically sound from experimental design to publication

KEVIN McCONWAY
16 March, 4.00–5.00pm

CLINICAL SKILLS WEBINAR

Management of acromegaly

JOHN AYUK & MARK SHERLOCK
25 March, 5.00–6.30pm

SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

Society members have free access to the current content of *Journal of Endocrinology*, *Journal of Molecular Endocrinology*, *Endocrine-Related Cancer* and *Clinical Endocrinology* via the members' area on the Society home page, www.endocrinology.org. *Endocrine Connections* and *Endocrinology, Diabetes & Metabolism Case Reports*, the Society-endorsed case reports publication, are open access and free to all.



JOURNAL OF MOLECULAR ENDOCRINOLOGY

Asprosin contributes to regulation of ovarian follicular function

Asprosin is a recently discovered protein encoded by the fibrillin-1 (*FBNI*) gene. It increases with fasting and decreases after feeding, and contributes to regulation of glucose metabolism. Elevated plasma asprosin is associated with an increased risk of developing polycystic ovary syndrome (PCOS). It directly correlates with androgen concentrations in women with PCOS who are obese, which may suggest that it has a role in regulating ovarian follicle androgen production. Asprosin and fibrillin are synthesised as a proprotein that is cleaved by the enzyme furin. Oocyte-specific deletion of furin leads to early follicle arrest and infertility in female mice, but whether asprosin has direct effects on ovarian function is unknown.

Maylem *et al.* assessed expression of mRNAs encoding *FBNI*, *FURLN* and *OR4MI* (the putative asprosin receptor 'olfactory receptor family 4 subfamily M

member 1') in granulosa and theca cells isolated from bovine ovaries. *FBNI* and *FURLN* were more abundant in theca cells than in granulosa cells, whereas the abundance of *OR4MI* was greater in granulosa cells, consistent with potential for paracrine asprosin signalling within follicles. Asprosin directly affected follicular function by enhancing luteinising hormone-induced androstenedione production. Asprosin also reduced insulin-like growth factor-1-induced theca cell proliferation, but did not affect progesterone production.

Together, these preliminary findings suggest asprosin signalling is present within the ovary and may contribute to regulation of follicular function.

Read the full article in *Journal of Molecular Endocrinology* **66** 35–44

ENDOCRINE-RELATED CANCER

Serine synthesis influences tamoxifen response in ER+ breast cancer

Oestrogen receptor-positive breast cancer (ER+ BC) accounts for 70% of all breast cancer cases. Growth of these tumours is driven by oestrogens, and endocrine therapies, such as tamoxifen, inhibit tumour growth by binding ERα and preventing proliferation. Although this is an effective therapeutic approach, endocrine resistance develops in 30% of ER+ BC, resulting in disease recurrence.

Phosphoserine aminotransferase 1 (PSAT1), an enzyme within the serine synthetic pathway, has been previously implicated in endocrine resistance. Metcalf and co-workers investigated expression of enzymes in the serine synthetic pathway in ER+ BC, in order to determine their potential role in endocrine resistance. The authors used transcriptomic data from patients with ER+ BC treated solely with tamoxifen, and found that elevated expression of

PSAT1 or phosphoglycerate dehydrogenase (PHGDH) was associated with decreased disease-free survival or relapse-free survival. *In vitro* studies using breast cancer cell lines representative of endocrine-sensitive (MCF7) or -resistant (LCC9) cancers demonstrated that the expression and activity of PSAT1 and PHGDH were higher in endocrine-resistant cell lines. When expression of PSAT1 was induced in MCF7 cells, tamoxifen-induced growth inhibition was reduced. Reciprocally, loss of PSAT1 or PHGDH in LCC9 cells restored tamoxifen sensitivity, and pharmacological inhibition of PHGDH in LCC9 cells sensitised them to tamoxifen.

These results suggest that overexpression of the serine synthetic pathway contributes to tamoxifen resistance in ER+ BC. Selective targeting may help to maintain endocrine sensitivity.

Read the full article in *Endocrine-Related Cancer* **28** 27–37

CLINICAL ENDOCRINOLOGY

Tertiary adrenal insufficiency in rheumatology patients on long term systemic glucocorticoids

Sagar *et al.* detail incidence, features and progression of rheumatology patients prescribed long term, high dose glucocorticoids. The work emphasises iatrogenic adrenal insufficiency by chronic glucocorticoid use (tertiary adrenal insufficiency) as a major contributor in withdrawal from medication and significant reductions in quality of life.

This retrospective study examined data from 238 patients, making it the largest of the few studies to examine glucocorticoid excess in a rheumatology patient group. Interestingly, adrenal insufficiency occurred in 43% of the patients (doses of prednisolone 5mg and above), a figure similar to comparative reports examining different patient cohorts. The pass-fail rate of a short synacthen test was unaffected by intramuscular glucocorticoids, suggesting oral steroids are the

primary source of risk of adrenal insufficiency, and also there was no benefit from switching to hydrocortisone to try and help weaning off steroids.

These are important data as they highlight the frequency of glucocorticoid-induced tertiary adrenal insufficiency in rheumatology patients. The findings are also in line with existing knowledge surrounding the inversely proportional relationship between peak glucocorticoid excess concentrations and chances of recovery. This work highlights the need for patient and healthcare professional education to minimise the risk of adrenal crisis for patients with hypothalamic-pituitary-adrenal axis suppression from exogenous steroids. As *The Endocrinologist's* Editor would say, 'Carry the steroid emergency card!'

Read the full article in *Clinical Endocrinology* doi:10.1111/cen.14405



THE COVER

Images for this edition's cover were kindly provided by Kate Lines, Mark Stevenson and Kreepa Kooblall from the University of Oxford.

The image in the top circle is of parathyroid adenoma cells stained for PTH (red) and DAPI (blue). The image in the middle circle (and background) is H&E staining of a mouse parathyroid gland, with surrounding skeletal muscle and some beautiful thyroid follicles.

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

The febrile patient with visceral ischaemia

Maung and co-authors present the case of an acutely unwell 22-year-old man. The primary presenting feature was severe abdominal pain, and the patient was haemodynamically unstable on admission, with a regular tachycardia, hypotension, fever and tachypnoea. He had central abdominal tenderness and guarding. Blood tests indicated acute kidney injury, and lactate was grossly elevated. Subsequent imaging showed evidence of mesenteric ischaemia, secondary to diffuse intra-abdominal venous thrombosis. Pulmonary embolus was also detected.

The underlying diagnosis was determined by the clinical signs of a goitre and dysthyroid eye disease, plus elevated free thyroid hormones and suppressed

thyrotrophin. The Burch–Wartofsky score was calculated as 60. The authors describe in detail the challenges of managing this man's thyroid storm, complicated by prolonged bowel ileus necessitating parenteral nutrition and therapeutics. Episodes of melaena made anticoagulation decisions difficult. Tests for genetic and acquired thrombophilias were negative.

The case serves as a valuable reminder of the hypercoagulable state that can result from thyrotoxicosis, and the authors discuss the role of prophylactic anticoagulation in thyroid storm patients, even those without tachyarrhythmia.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* doi:10.1530/EDM-20-0118

ENDOCRINE CONNECTIONS

Sleep deprivation, diet and human GH gene expression in transgenic mice

Serum levels of human growth hormone (hGH) vary considerably over a 24-hour period, in line with human behaviours. The impact of sleep duration on serum hGH has been documented, but specific transcriptional activation of GH has proved difficult to examine. This leaves questions regarding the mechanistic regulation of hGH expression in response to behaviour unanswered.

Jarmasz and colleagues have attempted to delineate the interactions between sleep and dietary regimens and the transcriptional control of hGH. The group used partially humanised transgenic 17hGH/CS mice, containing a single copy of the hGH gene. CD-1 mice were fed standard chow or a high fat diet as

well as being subjected to sleep deprivation protocols. The dietary regimen was unable to alter expression of circadian genes in wild type mice, whilst stress of acute sleep deprivation did change circadian expression. This demonstrates the uncoupling of dietary challenge from sleep deprivation. Additionally, for the first time, this study shows sleep deprivation to negatively impact hGH transcript levels in the pituitary.

The work suggests DNA methylation of the hGH gene as a putative mechanism for this regulation.

Read the full article in *Endocrine Connections* 9 1135–1147

ENDOCRINE HIGHLIGHTS

A summary of papers from around the endocrine community that have got you talking.

Reported allergic reactions and mRNA vaccines against COVID-19

Recent mRNA vaccine approval in the fight against COVID-19 has provided hope to millions around the world. However, for those individuals with a history of severe allergic reactions, the potential for vaccination is less certain. Current guidelines warn against mRNA vaccine administration to this patient group. Therefore, there is a clear need for risk stratification in regard to these individuals when assessing their likelihood of developing anaphylaxis.

To help guide clinicians and reassure those at risk, Banjeri *et al.* reviewed the current evidence surrounding anaphylaxis in response to the Pfizer–BioNTech and Moderna COVID-19 mRNA vaccines. The work summarised the rate of allergic reactions, which occurred at 1.3 per 100,000 doses, with severe events of fatigue and headache occurring at 3.8% and 2.0% respectively. Encouragingly,

hypersensitivity events occurred at a rate consistent with the placebo groups, suggesting that no component of the vaccines poses a risk. However, the authors do suggest the use of four screening questions to help evaluate risk level, and disclosure of a comprehensive list of vaccine constituents. It is also important to consider that vaccine administration is unlikely to always be performed by staff who regularly diagnose and treat anaphylaxis.

As rollout of the mRNA vaccines begins, administrators will have to remain watchful and ensure all groups have sufficient information and support to make an informed decision.

Read the full article in *Journal of Allergy & Clinical Practice* doi:10.1016/j.jaip.2020.12.047



No association between vitamin D and COVID-19 mortality

In the midst of the dark days of winter and the continuing COVID-19 pandemic, recent focus has been placed on the immunomodulatory role of vitamin D and its potential for influencing COVID-19 clinical outcomes. Low vitamin D is associated with increased likelihood of respiratory infections, but whether this impacts COVID-19 clinical progression is debatable.

A recent analysis by Lohia *et al.* assessed retrospective cohort data from 270 patients with COVID-19 infection and compared serum vitamin D concentrations with mortality, need for mechanical ventilation and admission to intensive care. Of these patients, 117 were male and 153 were female, more than half were aged 65 or older ($n=139$, 51.5%), the majority were African American ($n=216$, 80%) and more than a third had vitamin D levels below 20ng/ml ($n=95$, 35.2%). In the cohort and subgroup analysis, vitamin D levels showed no significant association with mortality, need for mechanical ventilation or admission to intensive care.

These data provide further insight, but the authors note that further studies are warranted before any conclusions can be made regarding any association between vitamin D status and clinical outcomes for COVID-19. Vitamin D is essential for good health and adequate intake via diet, supplementation and safe sunlight exposure along government guidelines are recommended to support bone and muscle health. Avoidance of vitamin D deficiency and adherence to COVID-19 guidelines remain the most robust approaches to minimising adverse risk to health (*BMJ Nutrition, Prevention & Health* doi:10.1136/bmjnp-2020-000089).

Read the full article in *American Journal of Physiology* doi:10.1152/ajpendo.00517.2020

TRANSFORMING METABOLIC BONE SERVICES IN THE PANDEMIC

WRITTEN BY NEIL GITTOES, ZAKI HASSAN-SMITH AND SHERWIN CRISENO



Redeployment of staff and refocusing of clinical activities during the height of the COVID-19 pandemic provoked crisis management, rapid service change and unprecedented opportunities for innovation in care delivery. Seeing through the haze of the crisis in March 2020 allowed recognition that there was impending significant risk to patients with pre-existing subacute and chronic illnesses, including large numbers of patients with bone and mineral diseases.

CHANGING AT PACE

Our metabolic bone service, including a fracture liaison service, supports a local population of 1.3 million and offers regional specialised bone and mineral network support to the broader conurbation (~6 million people). Early in the crisis, we risk-stratified patients and procedures, taking into account the benefits of our standard care pre-COVID versus the risks of COVID infection and of delaying our standard care. At pace, we adopted parallel streams of work to support patients locally and also at scale, through working with national organisations. The latter was important to provide standardisation of messaging and to avoid duplication of effort.

We used our databases to communicate with local patients individually by letter, in order to explain their illness in the context of COVID, along with any specific risks and advice. We also provided our rationale and reassurance regarding our adapted plans of care. Additionally, we signposted to other reliable sources of patient-focused information, including our own newly established endocrine-COVID helpline, which proved incredibly popular.

AN ENDOCRINE HELPLINE

Our endocrine helpline was set up to provide general and highly specialised advice and support to patients with endocrine conditions, during weekdays. The helpline, staffed by clinical nurse specialists and a consultant, also received queries from primary and community care colleagues, and from members of the public.

With most endocrine clinics cancelled, the helpline provided patients with a platform through which to access advice and support, including: enquiries on medication/dose adjustment (e.g. calcium dose adjustment in hypoparathyroidism during periods of illness, including COVID-19), prescription management, advice on employment/educational support, and arranging necessary follow-up consultations.

ADJUSTMENTS TO PATIENT CONTACT

We switched all routine face-to-face outpatient activities to telephone/video calls and rationalised our phlebotomy service to offsite locations. We also dramatically changed our thresholds for 'routine' bloods. All new referrals were actively triaged and, where possible, were addressed by advice and guidance. Furthermore, we adopted a 'forward look' approach to follow up and partial booking lists, and rationalised follow up and investigations according to clinical need.

We paused all intravenous bisphosphonate infusions due to the high risk of post-infusion systemic flu-like reaction and potential confusion with COVID-19 presentation. Following the end of the first lockdown, and with mass COVID testing being made available, bisphosphonate infusions were reintroduced in August 2020 and offered to both new and existing patients. A clear patient information leaflet was produced and given to all patients, informing them of the potential risk of 'flu-like' symptoms and need for COVID testing to rule out the infection.

Delayed denosumab treatment can result in rebound vertebral fractures, and so we adopted novel means of ensuring that patients already taking denosumab received their injections in a timely manner through domiciliary administration (local shared-care protocol), patient self-administration with support from clinical nurse specialists via video or telephone consultation

and, if required, hospital administration in a dedicated denosumab injection clinic. DXA (dual-energy X-ray absorptiometry) scanning was paused, as was the primary hyperparathyroidism pathway, including parathyroid surgery. Cases with extenuating circumstances were dealt with on an individual basis.

SHARING GOOD PRACTICE

In parallel to our local service response, we instigated pieces of work (internationally to provide repositories of information for clinicians and patients. Close working links with the Society for Endocrinology,¹ Royal Osteoporosis Society,² NHS England and NHS Improvement, NICE,³ patient support groups (e.g. Parathyroid UK⁴) and through academic publications,⁵ provided a means of sharing good practice while also 'reality checking' and learning the views and ideas of others within the field.

LESSONS LEARNED

We now have more efficient systems for triaging referrals, better use of remote follow up, with improved co-ordinated investigations to reduce outpatient 'visit' numbers (evidenced by a move towards a one-stop parathyroid service), a 'direct to infusion' offer and a proactive endocrine helpline service.

Although one size does not fit all, initial patient feedback is positive. It suggests that, for bone and mineral disorders (where many decisions are based on blood tests and scan results), patients perceive value in avoiding unnecessary travel to hospital with attendant costs and time, when a similar outcome can be delivered by a well-structured and two-way exchange, supported by some form of written communication. However, with rapid introduction of dramatic changes to service delivery, it is important to evaluate effectiveness and value to patients, the public and the care service as a whole, through audit and research. Patient satisfaction, impact of remote consultations and cost-effectiveness should be evaluated systematically.

Our ability to respond to COVID-19 has been borne out of close team working, open communication and visible leadership across administration, nursing and medical spheres. Our continued journey to innovate and refine care for patients with bone and mineral disorders will be shaped by listening to and responding to views of patients and working with patient groups and other stakeholders within our emerging integrated care system.

NEIL GITTOES

Consultant & Honorary Professor of Endocrinology, Head, Centre for Endocrinology, Diabetes and Metabolism, University Hospitals Birmingham NHS Foundation Trust

ZAKI HASSAN-SMITH

Consultant Endocrinologist, University Hospitals Birmingham NHS Foundation Trust

SHERWIN CRISENO

Advanced Nurse Practitioner & Lead Nurse - Endocrinology, University Hospitals Birmingham NHS Foundation Trust

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THE PANDEMIC, SEEN FROM A NURSE-LED OSTEOPOROSIS CLINIC

WRITTEN BY CAROLINE JAGGER AND WENDY ROWE



Around 3.5 million people over the age of 50 are affected by osteoporosis in the UK, with an estimated cost to the NHS of £4.5 billion per year.¹ It is estimated that one in five men and one in three women over 50 fracture bones due to osteoporosis. The most serious fracture types tend to be vertebral and hip fractures. These can be associated with problems such as pain, disability and sometimes even death.²

Osteoporosis specialist nurses are experts in the field of this and other bone conditions, and they have the benefit of being able to review patients in a timely manner, thereby increasing patient satisfaction. Patients can be directly referred to the service from both primary and secondary care. As osteoporosis nurses are autonomous practitioners, they can initiate tests, review and interpret results, prescribe treatments if required, monitor, and discharge where appropriate.³ This results in a service which benefits patients: in addition to being more accessible, specialist nurses can offer continuity of care and reduce the consultant burden.³

PRACTICALITIES OF RUNNING THE SERVICE

Our current nurse-led osteoporosis service operates from Monday to Thursday with two nurses (one band 6 and one band 7), covering seven clinics per week between them. A typical clinic includes new and follow-up patients.

For new patients, we would usually organise a bone density scan (dual-energy X-ray absorptiometry; DXA) and a variety of baseline blood tests. The initial consultation with the patient includes fracture history, past medical/surgical history, social history and a falls risk assessment. Once an individual's results have been reviewed and assessed, these are discussed with the patient and a fracture risk assessment (FRAX)⁴ is carried out. A plan of action is then mutually agreed with the patient. This usually incorporates oral, intravenous or subcutaneous treatments or monitoring only.

'As osteoporosis nurses are autonomous practitioners, they can initiate tests, review and interpret results, prescribe treatments if required, monitor, and discharge where appropriate.'

In the case of follow-up patients, DXA scans are usually performed every 2–3 years, or as often as clinically indicated. Patients are reviewed in clinic. Blood tests are usually carried out, including bone turnover markers, which indicate whether further treatment is needed or whether the patient can commence a treatment holiday. Treatments are evaluated for tolerability, efficacy and rare side effects, such as atypical femoral fracture and osteonecrosis of the jaw or auditory canal.

The osteoporosis specialist nurses refer patients to their local falls clinic if necessary. They also operate a telephone advice line, liaise with other members of the multidisciplinary team and attend meetings and conferences. Part of the role of the specialist nurse is health promotion, which includes dispensing advice such as regular weight-bearing exercise, plenty of dietary calcium and regular vitamin D supplements, as well as minimal alcohol and no smoking.^{5,6}

CHALLENGES EXPERIENCED

Working within the NHS can be challenging in terms of time, manpower, space, resources and workload, though the advent of COVID-19 has presented unprecedented challenges.

Pre-COVID-19, one of the challenges experienced in the nurse-led osteoporosis service was capacity – limited clinic space and a shared office. Other challenges included the telephone helpline: this is an excellent point of access for patients but, depending on the nature of the call, it can be time-consuming. Secretarial support can be variable, and letters dictated from clinic can be delayed by several weeks, which can delay management for patients who are being treated by their GP.

RISING TO THE COVID CHALLENGE

Due to the SARS-CoV-2 pandemic, all outpatient clinical activity was cancelled immediately. This led to a reduced service and redeployment of one member of staff to the COVID wards. The remaining osteoporosis nurse ran a basic service, ensuring treatments were delivered in a timely manner. The phone calls on the telephone helpline escalated during this time, as our patients were anxious and concerned about their diagnoses and treatments.

During the pandemic, when face-to-face clinic appointments were cancelled, GPs aided the delivery of our service. Some were able to offer blood tests and, due to a shared-care protocol, were able to organise and administer some 6-monthly injections of denosumab. This ensured the patient was not at an increased risk of vertebral fracture. Arrangements were made to deliver injections to the homes of patients who were able to self-inject. District nurses were organised to inject patients who were shielding at home. Occasional patients were given their injections in clinic if there was no viable alternative.

At the time of writing (early January 2021), we are mainly offering telephone appointments, with only around 20% of patients being seen face-to-face. However, due to the demographic of our patients, some are hard of hearing and do not like speaking on the telephone.

The benefit to the patient of a telephone appointment is that there is no travelling to a hospital site or problems with parking or locating the outpatient clinic. This reduces cancellations and pressures on hospital transport. Also, patients who are at risk and shielding avoid the risk of exposure to COVID-19 in the hospital.

GPs can undertake blood tests, and treatments can still be offered. However, GPs are unable to request measurement of bone turnover markers, and some are unable to test for vitamin D. This delays treatment, as patients must attend hospital for these tests. Additionally, osteoporotic patients are at a higher risk of fracturing their vertebrae and may need X-rays, which can only be offered after a physical review.

Overall, even with the difficulties experienced during the pandemic, the resilience of the staff and patients means that an expert service can still operate well, and provide safe and effective care for patients.

CAROLINE JAGGER AND WENDY ROWE

Osteoporosis Specialist Nurses, Manchester Royal Infirmary

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VITAMIN D AND CALCIUM: SUNSET FOR 'BUTCH CALCIUM AND THE SUNSHINE HORMONE'?

WRITTEN BY BO ABRAHAMSEN



Our patients have high expectations of what vitamin D supplements can achieve, but often express concerns about the safety of calcium tablets. We now have the advantage of several large new vitamin D trials, albeit with much less happening on the calcium front, yet the importance of calcium co-administration remains a dark horse here.

These trials continue to raise doubts as to what can be achieved by raising serum levels in populations that are already largely vitamin D-replete: i.e. with serum levels 50nmol/l or above, as proposed by the US Institute of Medicine.¹ Other thresholds have been proposed by other professional bodies, but with less persuasive arguments. The definition was based on skeletal outcomes, since there continues to be a lack of positive intervention studies for other outcomes (as we shall see below).

As endocrinologists, we also have to consider any realistic non-calcitropic effects of vitamin D, such as potential effects on thyroid autoimmunity, polycystic ovary syndrome, development of diabetes (including gestational diabetes; GDM), obesity, and the progression and complications of other endocrine disorders.

CALCIUM

In the anti-resorptive treatment area, some of the bisphosphonates have been evaluated without calcium supplementation, and the results have been good.² Thus, in patients on a dairy-rich Western diet who do not suffer from malabsorption or hypoparathyroidism, we may not need to rigorously enforce calcium supplements, though they have been co-administered in the majority of the original randomised controlled trials for osteoporosis drugs.

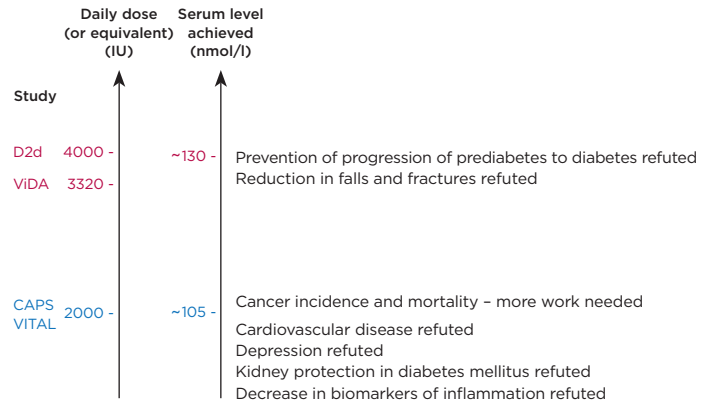
While avoiding calcium supplements in favour of dairy products seems intuitively right, there is no evidence that calcium supplements have a less favourable cardiovascular risk profile than dairy,³ and it is hard to understand why a phosphate-rich calcium source would be kinder to our vessels. However, calcium supplements can be followed by a transient spike in serum calcium, so repeating a serum calcium measurement in the fasting state, if initially raised in supplement users, saves time and work in the clinic.

VITAMIN D

There is genetic variability in the metabolism of vitamin D. This may require the occasional patient to require surprisingly high doses of vitamin D, especially initially, when fat stores are also being replenished. This aside, in the UK, the upper safe intake is considered to be 100µg (4000IU) daily, or ten times the 10µg (400IU) daily dose, which is the present supplementation in adults recommended by the Government.

COVID-19

The last few months have brought up the question of vitamin D in the prevention or treatment of COVID-19. In their 204-page rapid review, NICE and the Scientific Advisory Committee on Nutrition do *not* endorse vitamin D supplementation specifically to prevent or treat COVID-19, except as part of a clinical trial. Trials are in progress. The panel considered studies with primary outcomes being mortality, intensive care unit admission or hospitalisation. The panel also considered reviews of existing literature regarding vitamin D in preventing acute respiratory infections. Here, no protection was demonstrated in adults or when using vitamin D doses higher than 1000IU (25µg) per day.



Recent evidence on vitamin D supplementation has been disappointing in the cardiovascular, endocrine and musculoskeletal fields, but has shown a potential positive signal in the cancer area. ©Bo Abrahamson

Other fields

New evidence on vitamin D supplementation published in the last year or two has been fundamentally disappointing in the cardiovascular, endocrine and musculoskeletal fields, but has shown a potential positive signal in the cancer area (see Figure).

Large controlled vitamin D trials of 2000–4000IU daily (or equivalent but intermittent doses), capable of raising mean 25-hydroxyvitamin D (25-OHD) levels to above 100nmol/l, failed to reduce falls or fractures, failed to prevent cardiovascular disease, depression, progression from prediabetes to diabetes, and failed to offer kidney protection in diabetes or to decrease biomarkers of inflammation. Short term trials of the impact of vitamin D on lipid status have shown no effect or even a worsening.

Though the risk of GDM has been reported as being higher with vitamin deficiency, this may be due to confounding factors. It remains unclear whether vitamin D supplementation improves maternal or newborn outcomes in GDM, though smaller studies have been supportive, as recently reviewed elsewhere.⁴ The role of vitamin D deficiency in the development and prognosis of autoimmune thyroid disease is similarly controversial and interesting, but does not at present justify the use of vitamin D supplements in prevention or treatment of thyroid autoimmunity.⁵

The cancer findings are highly puzzling. The CAPS and VITAL trials both pursued cancer incidence as a primary outcome and the vitamin D dose used was 2000IU daily in both studies, over durations of 4 and 5.3 years respectively. Does calcium matter? The combination of calcium and vitamin D used in the CAPS trial resulted in a near-significant reduction in all-type cancer (hazard ratio (HR) 0.70, 95% CI 0.47–1.02, $P=0.06$), with significant findings in post-hoc analyses,⁶ while there was no signal at all in the VITAL study (HR 0.96, $P=0.47$).⁷ A recent meta-analysis supports an effect of vitamin D supplements on cancer mortality (five trials, RR 0.87 (95% CI, 0.79–0.96)), though no effect on cancer incidence.⁸

IN CONCLUSION

The role of vitamin D supplements in endocrine practice remains controversial, with new, large, randomised controlled trials failing to provide compelling evidence that even moderately high vitamin D doses, approaching the official upper safe limit of 4000IU (100µg) per day, lead to improved endocrine or metabolic outcomes in the general population. Intriguingly, cancer results looked more promising, where calcium was co-administered.

By nature, vitamin D is a threshold nutrient, and it appears increasingly unlikely that one size fits all, irrespective of baseline status. Thus, there could be vitamin D-deficient patient groups who benefit in terms of outcomes that were not significantly improved in the general, more replete, population. At present, the cancer arena offers more promise than the metabolic, endocrine or cardiovascular field as far as upper level doses of vitamin D in the general population are concerned.

BO ABRAHAMSEN

Professor, Consultant Endocrinologist, Department of Clinical Research, University of Southern Denmark, Holbæk Hospital, Denmark

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A more complete list is available from the author at babraham@health.sdu.dk.

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THE DAWN OF PARATHYROID HORMONE REPLACEMENT THERAPY

DAVID BAWDEN, WILLIAM D FRASER AND JEREMY TURNER



It is 99 years since Leonard Thompson was given an injection of bovine insulin. In the intervening decades, we have developed effective replacement therapy for the majority of the classical hormone deficiencies. With the advent of recombinant human parathyroid hormone (rhPTH(1–84); ‘Natpar’ in Europe or ‘Natpara’ in North America), we can finally complete the set.

VITAMIN D SUPPLEMENTATION

Conventionally, hypoparathyroidism has been treated by ‘bypassing’ the missing hormone and administering a pharmacologic mimic of one of its key downstream mediators. This takes the form of activated vitamin D as 1 α -hydroxylated vitamin D (alfacalcidol) or 1 α ,25-dihydroxylated vitamin D (calcitriol), and is given with supplemental calcium.

The hydroxyl group in the 1 α position (Figure 1) is the crucial molecular feature in activating vitamin D and enabling it to bind to the vitamin D receptor (VDR) and activate downstream signalling. One role of PTH is to regulate the hydroxylation of vitamin D at this location, to effect activation (Figure 2). Since PTH is a peptide hormone which is normally poorly active or completely inactive via the oral route, administration currently must be via a parenteral route. Few people like injecting themselves and, historically, the alternative (1 α -hydroxylated vitamin D metabolites with or without calcium) that is orally bioavailable has assumed primacy.

ASSOCIATED DRAWBACKS

However, there are numerous and significant drawbacks to the treatment of hypoparathyroidism with activated vitamin D and calcium. These include:

- a slow onset of action
- a prolonged duration of action
- difficulties with accurately titrating the dose and, most fundamentally,
- as this is not actual hormone replacement therapy, the missing hormone’s actions are not all accurately reproduced.

While PTH reduces tubular calcium excretion, alfacalcidol and calcitriol (especially in combination with oral calcium salts) are associated with

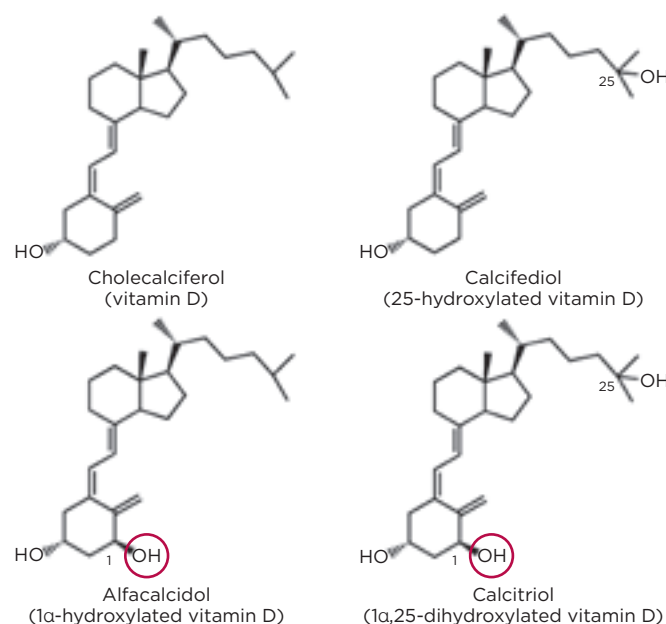


Figure 1. Molecular structure of ‘plain’ vitamin D, calcifediol (25-hydroxylated vitamin D), alfacalcidol (1 α -hydroxylated vitamin D) and calcitriol (1 α ,25-dihydroxylated vitamin D), highlighting the 1 α -hydroxyl group.

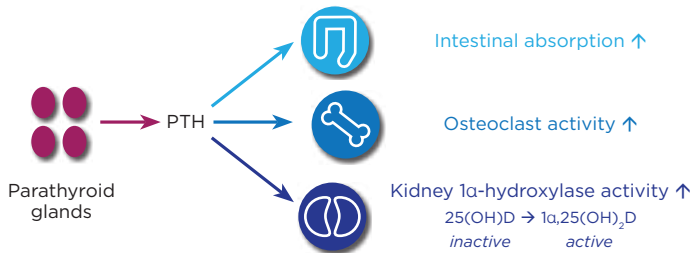


Figure 2. PTH secreted from the parathyroid glands stimulates 1α-hydroxylase in the kidneys to activate 25-hydroxylated vitamin D to 1α,25-dihydroxylated vitamin D.

hypercalciuria, causing significant risk of nephrocalcinosis, nephrolithiasis and renal failure.^{1,2} Difficulties with titrating the dose of activated vitamin D compounds, combined with a perception that these are ‘only’ a vitamin (and by implication must be harmless), mean that many patients treated with these compounds have received less specialist attention³ and less intensive medical supervision and biochemical monitoring than required. This, in turn, is associated with a significant incidence of severe iatrogenic hypercalcaemia and demonstrable patient harm, leading the former National Patient Safety Agency to issue a safety alert about alfacalcidol.⁴ In addition to all these considerations (and arguably, most importantly of all), many with hypoparathyroidism treated with activated vitamin D-based regimens experience poor quality of life and frequent unplanned hospital attendances for hypo- and hypercalcaemia.³

There is, therefore, a very real and clear need for improved treatments for hypoparathyroidism.

RECOMBINANT HUMAN PTH

What could be better than actual hormone replacement therapy? Recombinant PTH(1–84) is now licensed as a treatment for hypoparathyroidism in Europe, North America and other regions, but how did we get here, and what are the ongoing challenges yet to be resolved with this treatment?

rhPTH(1–34), originally teriparatide, now biosimilars such as Movymia, is licensed for the treatment of osteoporosis. However, long before its licensing for osteoporosis, attempts were made to augment treatment of hypoparathyroidism with subcutaneous teriparatide injections and, later, subcutaneous teriparatide infusion therapy. The earliest report dates back to 1986.³ Initial experience was encouraging, including (importantly) reductions in urinary calcium excretion. Many reports have confirmed these favourable outcomes.^{6,7}

In 2013, the results of the first large randomised controlled trial (RCT) of full length rhPTH(1–84) for treatment of hypoparathyroidism (REPLACE) were published.⁸ Since then, results of other RCTs have been published,^{9–11} by and large confirming the favourable safety and efficacy profile of rhPTH(1–84) as a treatment for hypoparathyroidism.

Favourable effects include reduced calciuresis, improved quality of life, reduced activated vitamin D and oral calcium supplementation dose requirements and improved bone turnover marker profiles. These suggest that, in the long term, there may also be favourable effects on fracture risk and other aspects of skeletal health from PTH replacement therapy. High rates of attainment of normal albumin-adjusted serum calcium levels are also seen in such RCTs.

There is a theoretical concern about osteosarcoma, but this signal is derived from rodent data. In nearly 15 years of post-licensing/‘real world’

use of teriparatide, where the same concern pertains, there has been no significant confirmation of this signal in human clinical use. In excess of 5 years’ trial data for rhPTH(1–84) are now available. Thus far, they are very reassuring.

Typical rhPTH(1–84) doses range between 25 and 100µg, given as a once daily subcutaneous injection. They are usually given in combination with oral calcium supplements and activated vitamin D, although some individuals can achieve normocalcaemia without oral supplements.

Development of an oral preparation of PTH(1–34) is also underway, where gastric degradation of the peptide is prevented by a combination of chemical/physical protection. This has entered preliminary trials in hypoparathyroidism which have resulted in promising results. This development may help overcome the fear of self-injection of PTH.

IN CONCLUSION

Nearly 100 years after the dawn of the hormone replacement era, endocrinologists are finally seeing the availability of hormone replacement therapy for hypoparathyroidism. This is only the beginning, and many unanswered questions remain about the optimal use of this treatment. The field is still evolving, and many patients are likely to remain on conventional activated vitamin D plus oral calcium supplementation therapy for some time.

Even for those lucky enough to have the option of rhPTH(1–84) therapy, it should probably mainly be seen as an adjunct for now, to be used alongside activated vitamin D and oral calcium supplements. There is certainly more work to be done!

DAVID BAWDEN

Specialist Registrar in Endocrinology,
Norfolk and Norwich University Hospital

WILLIAM D FRASER

Professor of Medicine and Dean of Medical School,
University of East Anglia

JEREMY TURNER

Consultant Endocrinologist and Honorary Professor, Norfolk and
Norwich University Hospital and Norwich Medical School

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PARATHYROID CALCIUM SENSING JUST GOT MORE COMPLEX

WRITTEN BY CAROLINE GORVIN



The parathyroid glands have a critical role in regulating serum calcium concentrations by secreting parathyroid hormone (PTH). Almost 30 years ago, the G protein-coupled receptor (GPCR) that allows parathyroid glands to detect serum calcium concentrations was cloned from bovine parathyroid tissue and named the calcium-sensing receptor (CaSR). Studies since then have helped us understand that calcium binding to the extracellular surface of the CaSR triggers receptor conformational changes, activation of associated G proteins and their downstream signalling pathways and, ultimately, suppression of PTH secretion.

The CaSR is able to couple to all four G protein family subtypes, but predominantly activates two families, $G_{q/11}$ and $G_{i/o}$, to stimulate intracellular calcium mobilisation and MAPK pathways, and reduce cAMP production. Studies in the past 10 years have, however, revealed complexities within the CaSR signalling system and expanded our understanding of calcium homeostasis (Figure).

CaSR MUTATIONS DISRUPT CALCIUM HOMEOSTASIS

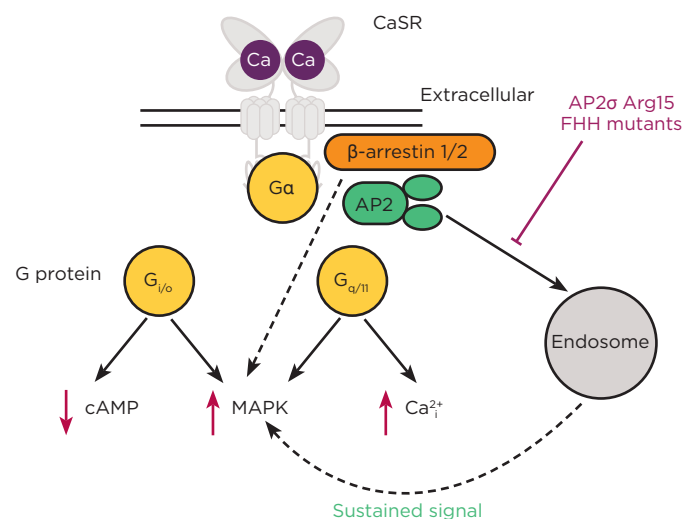
The publication of the CaSR gene sequence led to a rapid succession of manuscripts describing mutations in the receptor associated with disorders of calcium homeostasis. It is now understood that inactivating mutations cause familial hypocalciuric hypercalcaemia (FHH) and, rarely, neonatal severe hyperparathyroidism, which can be fatal if untreated.^{1,2} In contrast, activating CaSR mutations cause autosomal dominant hypocalcaemia (ADH). Although benign in many cases, CaSR mutations can cause symptoms in some patients including muscle cramps, kidney stones, chondrocalcinosis and seizures.^{1,2}

The investigation of CaSR mutations *in vitro* has been important in confirming their pathogenicity, but has also revealed individual residues that play critical roles in CaSR receptor activation. These include residues located in the receptor homodimer interface and transmembrane regions, at which both activating and inactivating mutations have been identified. These residues, termed 'switch residues', are hypothesised to act as molecular switches that undergo conformational changes on ligand binding, and their mutation facilitates receptor structures that preferentially signal via Ca^{2+} or pERK pathways³ (i.e. they 'bias' signalling). Additionally, other CaSR mutations have been described that bias signalling towards G protein-independent β -arrestin pathways.⁴ The physiological effect of CaSR signalling by these specific pathways remains to be explored in detail, but could allow the design of CaSR-targeting compounds with fewer side effects.

MUTATIONS IN THE PATHWAY CAUSE HYPER-/HYPOCALCAEMIA

While CaSR mutations are the most common cause of FHH and ADH, a subset of patients have mutations in other proteins that function within the CaSR signalling and trafficking pathways.² Both inactivating and activating mutations have been identified in the gene encoding $G_{\alpha_{11}}$, through which CaSR signals. These mutations cause a milder form of FHH, attributed to the ability of CaSR to compensate for loss of $G_{\alpha_{11}}$ signalling by coupling to other G proteins. This could explain why patients with $G_{\alpha_{11}}$ mutations do not present with a wider range of symptoms, despite numerous GPCRs with critical roles in the cardiovascular and central nervous systems utilising $G_{\alpha_{11}}$ signalling. Detailed studies of G protein signalling in the presence of mutant $G_{\alpha_{11}}$ are required to better understand this.

Perhaps most intriguingly, mutations in the σ -subunit of the adaptor protein-2 (AP2) also give rise to FHH. AP2 is a heterotetrameric protein that plays a fundamental role in clathrin-mediated endocytosis, a



The CaSR can activate G protein-signalling pathways downstream of the G proteins $G_{i/o}$ and $G_{q/11}$, leading to cAMP reductions, and increases in calcium mobilisation and MAPK signalling. Mutations in the CaSR, $G_{\alpha_{11}}$, and AP2 σ proteins cause disorders of calcium homeostasis. Studies of these mutations have revealed that CaSR can signal via a G protein-independent pathway involving β -arrestin and can signal from within the cell following endocytosis (sustained signal). FHH, familial hypocalciuric hypercalcaemia. ©Caroline Gorvin

process required by cells for nutrient uptake and internalisation of transmembrane proteins. AP2 σ is the smallest subunit of the AP2 complex, and mutations in FHH patients affect a single residue, Arg15. Previous studies show that this residue is important for binding to internalisation motifs within transmembrane proteins. We therefore hypothesised that FHH mutations in Arg15 must affect binding of AP2 σ to CaSR, and thus affect CaSR internalisation. Indeed, studies of CaSR trafficking using total internal reflection fluorescence microscopy demonstrated an impairment of CaSR endocytosis in cells expressing FHH-associated AP2 σ mutations, and consequently increased CaSR cell surface expression.³ However, AP2 σ mutations reduce CaSR-mediated signalling. At first, this appeared paradoxical, as more receptor at the cell surface should equate to more signalling by the receptor. So, how are the AP2 σ mutations impairing CaSR signalling?

To uncover the molecular mechanisms, we turned to other GPCRs as a guide. Some GPCRs, including thyrotrophin and PTH receptors, can continue to signal once internalised.⁶ We hypothesised that the CaSR may also have long-lasting cytoplasmic signals, and that depletion of internalised CaSR by the AP2 σ mutations would reduce signalling from this source. Using a combination of imaging techniques, signalling assays

and inhibitors of endocytosis, we showed that CaSR can signal from an internal location that is likely to be endosomal.⁵ Furthermore, this internalisation-dependent pathway involves only G_{q/11} signalling and, therefore, these studies demonstrate how a single GPCR can resolve pleiotropic signals by spatially directing G protein selectivity.

REMAINING QUESTIONS

Elucidation of these novel CaSR signalling pathways has uncovered new mechanisms by which the receptor signals. However, they have generated important outstanding questions, such as:

- what are the physiological functions of CaSR endosomal signalling?
- does endosomal signalling take place in all CaSR-expressing cells?

Further research focused on answering these questions may help facilitate the development of targeted therapies, to activate sustained endosomal

signalling in a biased manner. This could provide novel pharmacological treatments for a range of hyper- and hypocalcaemic disorders.

CAROLINE GORVIN

Institute of Metabolism and Systems Research,
University of Birmingham

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MANAGING HYPOPARATHYROIDISM: A SHARED ENDEAVOUR



WRITTEN BY LIZ GLENISTER

Parathyroid UK has nearly 3,500 members, of whom 75% have permanent hypoparathyroidism. When I set up our organisation, this rare condition was largely unrecognised. Today, it is more widely known, but remains quite poorly understood and no less difficult to manage.

MY STORY

In 1992 I went into hospital to have a total thyroidectomy for papillary thyroid cancer. I came out thankfully cured of cancer, but with incurable hypoparathyroidism instead. The hypocalcaemic seizure I had 3 days later was so severe that I needed post-traumatic stress counselling. Unable to stabilise me, my surgeon referred me to an endocrinologist, but my calcium levels were never to settle down. Finally, I was told that I was 'bringing symptoms on myself' and discharged.

For the next few years, I was engaged in a solitary battle for survival and information. I had to fight for the treatment and monitoring I needed. Eventually, I met my seventh consultant, the first with experience of managing hypoparathyroidism. He agreed that I had been severely under-treated, and life began to improve.

LACK OF AWARENESS

Sadly, despite our awareness-raising efforts and the rise of interest in rare disease, this quest for understanding is still part of life for many patients today. We are hugely grateful to our wonderful advisors,¹ who dedicate so much time to education, and to those who learn from them. However, the fact remains that standards of care vary widely, and the reality is a sobering picture indeed. While lack of experience of patients with rare diseases is understandable, it is distressing for patients to encounter a lack of willingness to learn about their condition.

THE NEED FOR SELF-MANAGEMENT

Once diagnosed, the most challenging issue for patients is the daily management of calcium levels. Calcium can fluctuate in response to a myriad of events, yet blood tests are not always accessible. Results take too long when symptomatic, and GPs often have no guidance from consultants. Left to self-manage between appointments, people turn to support groups.

We have found that educating patients on how to self-manage, as far and as safely as they can, is necessary to avoid crises. We follow guidelines and our specialists' advice, and we also inform patients about the 'no or low calcium' protocol,² which has led to great improvements.

Patients are always asked to talk to their doctor, but they are also given appropriate lifestyle advice and can learn about the condition itself: how to recognise symptoms, and how and when to take action if necessary. We direct the urgent cases to A&E; there are too many of these, and we feel anxious and burdened by this responsibility. While some self-management is unavoidable, we need our doctors to have a good understanding of the demands upon us.

UNDERSTANDING MANAGEMENT GOALS

Crucially, the aim is to maintain serum calcium at a high enough level to prevent symptoms, but low enough to protect renal health. And herein lies the hypoparathyroidism Sisyphean task.

Patients can feel very symptomatic within the normal reference range. Most have their own level where they feel comfortable and symptom-free. This level may be above the recommended goal but, as stated at the Society for Endocrinology BES conference last year, if kidney function permits, allowing the patient to maintain calcium at this level can make a huge difference to their quality of life.

Compounding this problem is the lack of understanding around vitamin D. Patients are still frequently told that they don't need vitamin D₃, because they are already on alfacalcidol or calcitriol. We do. The need for us to take vitamin D₃ (and magnesium) is enshrined in the European Society of Endocrinology guidelines³ and is reiterated by our advisors, so receiving conflicting advice is very confusing for patients. A patient with normal calcium can feel symptomatic due to low vitamin D or magnesium levels. Sufficient levels of alfacalcidol, vitamin D₃ and magnesium allow us to get the calcium we need from our diet, which improves stability and reduces hypercalcaemia.

Changes to medication must be made incrementally. In our support groups, we see people suffering the consequences of mismanagement every day. People are regularly being admitted to hospital because their medication has been over- or under-adjusted: a distressing experience that can be avoided. Even tiny changes in medication can cause dramatic changes in symptoms.

Emergency care, too, needs consideration. Patients need access to urgent blood test results, a plan of action and an emergency contact. We have now produced an emergency medical card, but a consultant's letter would ease A&E visits considerably.

SHARED GOAL SETTING AND DECISION MAKING

After 28 years, my levels have never properly stabilised, yet I feel very fortunate because I have a consultant who listens, reflects, understands my need to feel as good as I can and works with me to find ways to meet that. He recognises that effective management needs to be, as far as possible, a joint endeavour. Mutually respectful, shared, goal setting and decision making can lead to improved outcomes and a better relationship.

However, we are still dependent on our doctors to get things right for us, so I urge you to learn all you can about the condition: read the guidelines,³⁻⁵ attend the Society for Endocrinology Clinical Updates, visit our website (www.parathyroiduk.org) and our (virtual) stand at conferences, and work with us to help lessen the daily impact of hypoparathyroidism on our lives. In a shared endeavour we all have an important role to play.

LIZ GLENISTER
Founder and Chief Executive
(Volunteer) at Parathyroid UK

You can find out more about
Parathyroid UK at www.parathyroiduk.org
or on
Twitter @ParathyroidUK.



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THE BONE AND CALCIUM ENDOCRINE NETWORK: OUR TIME AS CONVENORS

WRITTEN BY CAROLINE GORVIN AND JEREMY TURNER



As co-convenors, we have led the Society for Endocrinology's Bone and Calcium Endocrine Network since 2018. Our initial vision for the Network was as a place where all members of our community (researchers, clinicians, nurses and patient support groups) felt welcome and could engage in conversation about academic and clinical practice in our exciting field of endocrinology.

OUR ACHIEVEMENTS SO FAR

We aspired to bring effective leadership to the Bone and Calcium Network, whilst also very much recognising that we are only two voices in a much larger forum. With this in mind, we began our tenure by seeking the opinions of our members via online surveys, and providing regular updates to our members via newsletters. We have also recently launched our Network Twitter account; we encourage everyone to follow [@bonenetwork](#) and share content.

For our meetings at the Society for Endocrinology BES conferences, we have tried to deliver a mixed programme made up of:

- inviting members to pitch ideas, which has been successful in forming new collaborations
- having invited speakers (i.e. a 'big name' to draw in the crowds), and
- holding an open discussion.

A key aim was to make sure patients' perspectives were heard at all our meetings. We are proud to have worked closely with Liz Glenister of Parathyroid UK to achieve this.

We are unlikely to be alone in thinking that one of our most important achievements was canvassing, alongside convenors of other Networks, to move the timing of the Network meeting slots at SfE BES from their original pre-08.00 location to after lunch. This has allowed greater attendance and engagement at these sessions.

PROGRESS IN 2020

We had several events planned for 2020, which unfortunately were postponed or re-organised as virtual meetings. Together with some of our nurse and clinical members, we were looking forward to hosting our first Specialist Nurse Research Training Meeting in April 2020. We still hope we can deliver this content in a virtual meeting in 2021, allowing more nurse members to participate.

Similarly, many members were planning to attend the Society for Endocrinology-endorsed Gut–Bone Axis Meeting, organised by Jeremy Turner and Nikki Horwood, that was promoted by the Network. Like so many meetings in 2020, this was postponed and will be delivered online in 2021.

Our biggest Network task for 2020 was planning our virtual meeting for SfE BES 2020. We quickly realised that our usual informal open discussion would be impossible, as most content had to be prerecorded. Being aware of growing 'online meeting fatigue', we tried to plan an event that would appeal to as many members as possible, with both a basic science and a clinical talk covering new studies in the bone and calcium field.

We couldn't ignore the impact of COVID-19 on clinical practice, and Neil Gittoes (Birmingham) gave a fantastic presentation on the clinical guidelines

that he and his colleagues published this summer in *European Journal of Endocrinology*, giving guidance on management of calcium metabolic disorders and osteoporosis.¹

In our second talk, Donald Ward (Manchester) presented some of his group's recent basic science studies on phosphate sensing. Published in late 2019 in *Nature Communications*,² these studies demonstrate a role in phosphate sensing for the calcium-sensing receptor, which has long been known to regulate calcium homeostasis.

We are extremely grateful to our speakers for giving up their time to record these talks and for their engagement in the live Q&A sessions afterwards. We were pleased to learn from the Winter 2020 edition of *The Endocrinologist* that our session was one of the top 10 attended sessions. Content from the meeting is still available online in the Members' Area of the Society for Endocrinology website.

'We are especially excited about plans for online Network meetings, in which researchers will be able to submit abstracts and give short presentations.'

OUR VISION FOR THE FUTURE

While it remains difficult to predict what the future holds under the current circumstances, we are hopeful we will be able to continue to provide new opportunities for members to network over the coming year. We are especially excited about plans for online Network meetings, in which researchers will be able to submit abstracts and give short presentations. This is particularly important for our early career members, many of whom are students, and have missed those important opportunities to present and get feedback on their work.

We are always happy to hear ideas from our members about new strategies to encourage discussion, or content for our meetings; contact us at networks@endocrinology.org. We look forward to seeing all members of the endocrine community face-to-face at future meetings.

Finally, we could never have achieved any of this without the fantastic support of the Society for Endocrinology, especially Rachel Austin, who has been amazing at helping to organise meetings, and turning our ideas into perfectly formatted newsletters.

CAROLINE GORVIN

Institute of Metabolism and Systems Research,
University of Birmingham

JEREMY TURNER

Norfolk and Norwich University Hospitals

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Introducing **THE SfE SKILLS ACADEMY**

The Society for Endocrinology is excited to announce a complete programme of virtual training events to support our members throughout 2021.

FOR EARLY CAREER RESEARCHERS

RESEARCH SKILLS WEBINARS

This series will continue to focus on techniques for research and analysis whilst access to laboratories remains limited. With pre-recorded content and live Q&A sessions, it is an opportunity to join in and learn from experts, to help further your research. The first webinar is on **16 March 2021**; further information will be provided on the website in due course. To see what you may have missed, catch up on the Research Skills Webinars from 2020 by logging in to the Society for Endocrinology Members' Area at www.endocrinology.org.

ENDOCRINE NETWORK-LED PRESENTATIONS

Join peers, present your research and network with established endocrinologists at the Endocrine Network-Led Presentations, which will launch in mid-2021. To continue our support to you during these difficult times, these sessions will provide an opportunity to share your research, expand your range of contacts and sow the seeds of future collaborations.

CAREER SKILLS SESSIONS

The Society is proud to introduce interactive Career Development Training Days to support your personal development. These will focus on practical skills to further your career, and will include live Q&A sessions.

FOR CLINICIANS

CLINICAL SKILLS WEBINARS

The Society is pleased to announce that the valuable Clinical Skills Webinar series will continue for 2021. The first webinar is available to stream on demand now in the Members' Area and the next session is on **25 March 2021**. The content will support those sitting the MRCP(UK) Specialty Certificate Examination in Endocrinology and Diabetes, as well as clinicians and nurses at all stages of their career who require continued professional development. Registration is free for members and the webinars will be streamed monthly throughout 2021: www.endocrinology.org.

FOR NURSES

ENDOCRINE NURSE SKILLS WEBINARS

After the successful launch of the Endocrine Nurse Skills 2020 Webinars, the Society will continue to deliver essential training for Nurse Members. The Endocrine Nurse Skills Webinar 2021 series will provide all the latest updates and support for professional development.

OTHER EVENTS

NATIONAL CLINICAL CASES ONLINE

National Clinical Cases will be taking place virtually during summer 2021. Presentation of ten unique cases will be followed by a live Q&A session. The online format will continue to provide an opportunity for trainees and junior colleagues to share challenging cases with senior endocrinologists from across the UK.

SfE BES 2021

We are intending to meet in-person in Edinburgh during the winter of 2021. Inevitably, we have a contingency plan, should our face-to-face event not be possible. We will, once again, provide you with the best endocrine science, and the opportunity to participate alongside peers, contemporaries and friends. To watch any of the talks from SfE BES Online 2020, please log in to the Members' Area at www.endocrinology.org.

ADDITIONAL INFORMATION

All webinar series which took place in 2020 and SfE BES Online are now available to stream on demand, free of charge, via the Members' Area at www.endocrinology.org.

A PLACE FOR CoMICs IN MEDICAL EDUCATION

WRITTEN BY EMILY WARMINGTON, DANIA SHABBIR AND PUNITH KEMPEGOWDA



The practice of evidence-based medicine requires healthcare professionals to stay up-to-date with an ever-growing body of medical literature. Medical students and junior doctors are frequently overwhelmed by the sheer volume of information available to them when learning about medical conditions. The vast majority of this is presented as reams of text in books or online. Such material can seem inaccessible, causing stress and deterring many from engaging with the latest research.¹

Several studies have demonstrated the efficacy of infographics (defined as the 'utilisation of images and data visualisation to present research in an engaging way'²) in communicating complex information to students, both in the medical field and more generally.^{3,4} Information presented visually is processed more quickly than simple text, and allows students to remember up to 6.5 times more information than words alone,⁵ improving long term memory and retention. Furthermore, the current climate of the COVID-19 pandemic has served to highlight the need for provision of robust online teaching resources. Social media, in particular, is an increasingly effective tool for increasing exposure to, and knowledge of, medical information on a global scale.⁶

It was in this context that a team of like-minded individuals, from a range of backgrounds and nationalities, came together with an innovative vision: to change the delivery of medical education and help people worldwide understand medicine more easily through short, comprehensible videos. Thus, Concise Medical Information Cines (CoMICs) was born.

INTRODUCING CoMICs

CoMICs is a new medical education initiative conceptualised by Punith Kempegowda from the University of Birmingham's Institute of Metabolism and Systems Research and led by Nia Evans, a junior doctor from Royal Glamorgan Hospital, north west of Cardiff. CoMICs comprises bite-sized videos consisting of illustrations and infographics created by medical students and junior doctors. Whiteboard animations are used to simulate traditional classroom teaching and to keep viewers engaged with the content.

Each CoMIC depicts a specific disease or medical condition, from presentation and investigations to stepwise management and follow-up options. The information on each topic is based on national and international guidelines, presented at an easily intelligible level and reviewed by early career researchers and experts in the relevant field from both the UK and internationally. This ensures that the contents of the video are not only easily digestible, but accurate and based on the most up-to-date research. CoMICs is tightly intertwined with SIMBA (Simulation via Instant Messaging - Birmingham Advance), our sister organisation, which aims to provide interactive, simulation-based learning through instant messaging for medical education (see opposite).

CREATING CoMICs

The process of creating a CoMIC consists of five steps. A medical condition is identified by a member of the CoMICs team; the selected disease is based on the simulated cases used during SIMBA sessions. Then, a medical student is invited to create a video script. A member of the CoMICs team uses this script to create a short (<5 minute) animated video. Once made, this video is critically reviewed by early career researchers and world-renowned experts with a special interest in the relevant field, to ensure the accuracy and clarity of its contents. The finalised video is then



Example from a CoMICs video. ©CoMICs

shared publicly on various social media platforms: YouTube, Instagram, Twitter and Facebook.

The medical students and junior doctors involved in the creation of CoMICs gain invaluable experience in medical education, revision of key concepts and the opportunity to work directly with leaders in the field. Guest CoMICs reviewers also get the chance to contribute to an exciting initiative which is growing in popularity each week, and will be fully credited for the video they contribute to. Applications for guest CoMICs reviewers are now open, and early career researchers from around the world are encouraged to apply.

A new video is shared every week as part of our #CoMICWednesday initiative. So far, 25 episodes have been released, covering various complex topics in the field of endocrinology and diabetes (amongst others), to a positive response.

For more information and to watch our previous CoMICs, please visit our web page (<http://bit.ly/SimbaComics>) or follow us on social media: YouTube (**SIMBA Simulation**), Twitter (**@SimbaComics**) and Instagram (**@simba.comics**).

EMILY WARMINGTON

4th Year Medical Student, University of Birmingham Medical School

DANIA SHABBIR

5th Year Medical Student, Jinnah Medical College, Pakistan

PUNITH KEMPEGOWDA

Honorary Specialist Training Registrar in Endocrinology, Diabetes and General Internal Medicine, University Hospitals Birmingham NHS Foundation Trust, and Wellcome Trust Clinical Research Fellow, Institute of Metabolism and Systems Research, University of Birmingham

on behalf of the CoMICs team

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SIMBA: SIMULATION-BASED LEARNING, CREATED BY AND FOR STUDENTS AND JUNIOR DOCTORS

WRITTEN BY ANISAH ALI, DENGYI ZHOU AND PUNITH KEMPEGOWDA



Simulation-based medical education (SBME) is increasingly becoming recognised amongst healthcare students and professionals. SBME can be defined as an educational activity, using simulation to replicate a clinical scenario.¹ Providing an alternative to real patients allows trainees to develop their knowledge, skills and attitudes in a comfortable environment, without putting patients at unnecessary risk.²

‘Simulation via Instant Messaging – Birmingham Advance’ (SIMBA) incorporates SBME into medical teaching.³ The aim of SIMBA is to create simulations based on real life situations, using minimal and existing resources to improve healthcare professionals’ confidence. It is a global initiative created by Punith Kempegowda and Eka Melson from the University of Birmingham’s Institute of Metabolism and Systems Research and led by medical students and junior doctors. The model utilises free and easily accessible platforms – WhatsApp and Zoom – enabling international participation.

Transcripts are created based on real life scenarios, starting from history and examination, through to investigations and management plans. Participants then work through these simulated cases, moderated mostly by medical students. At the end of the session, participants and moderators join an interactive Zoom call, where an expert discusses the most important aspects of each case, focusing on the rationale for decision making. Participants interact and ask questions pertinent to the cases and consolidate their knowledge during this discussion. A certificate of attendance is linked to the

end of the feedback survey. Feedback on performance, based on an adapted version of the global rating scale, is sent to all participants within a week of the session.

SIMBA INCREASES CONFIDENCE

From 3 July 2019 to 3 October 2020, six successful SIMBA sessions were held on different aspects of endocrinology or diabetes. These included Pituitary 1.0, Diabetes 1.0, Adrenal, Thyroid, Pituitary 2.0 and Diabetes 2.0. Participants completed pre-SIMBA and post-SIMBA questionnaires, rating their confidence levels on the management of clinical cases, related to the respective session topics. Confidence levels were measured using a Likert scale ranging from strongly disagree to strongly agree. Participants also provided qualitative feedback via open-ended questions on the competency areas they improved on.

The responses were anonymised, combined and categorised into three categories: (i) confident (strongly agree, agree), (ii) unsure (agree somewhat, undecided and disagree somewhat), (iii) non-confident (disagree, strongly disagree). Results were analysed using Stata (www.stata.com), to compare trainees’ confidence levels pre- and post-simulation. The results are reported using percentages and displayed in bar charts (see Figure).

There was an overall significant improvement in trainees’ self-reported confidence levels in all six sessions. The sessions Adrenal, Thyroid, Pituitary 2.0 and Diabetes 2.0 showed statistically significant improved confidence levels ($P < 0.0001$), as did Pituitary 1.0 and Diabetes 1.0 ($P = 0.0002$).

SIMBA IMPROVES KNOWLEDGE

Common themes identified from open-ended questions on the areas that participants had improved upon post-session were patient care, knowledge of patient management and practice-based learning. Overall,

Changes in confidence levels before and after SIMBA across six different sessions. ©SIMBA



our participants felt more confident in ordering relevant investigations, and taking a systematic and individualised approach to managing specific cases.

Medical students as moderators also benefited from the sessions. Acting as a moderator allows students to familiarise themselves with the structure of taking an effective history and suggesting relevant examinations, investigations and management plans.

OTHER BENEFITS OF SIMBA

As well as developing medical knowledge, SIMBA promotes teamwork and leadership skills amongst medical students. Each specialty stream within SIMBA consists of a core moderator team. Within the team, a stream lead will oversee the roles of other members, encouraging decision making and mentorship. Each team member has a specific allocated role, working towards a set deadline. Attentive and consistent communication is required, to ensure conformity is reached across the team. Time-management skills are developed through the need to prioritise tasks and work co-operatively to ensure deadlines are met.

Students also lead moderator-training sessions, which is a chance to further develop their communication skills. Efficient planning and co-ordination are necessary to ensure sessions run smoothly and any difficulties are raised and resolved. Students are further encouraged to provide feedback and constructive criticism, enabling peer learning and teaching.

Medical students' feedback revealed they felt self-assured in seeking new leadership and team roles within their medical school as a result of SIMBA. They felt more confident in working with senior colleagues, articulating their thoughts and communicating with clarity. The use of online platforms such as WhatsApp and Zoom has eased students into utilising online communication for medical education. It also promotes international collaboration, with the SIMBA team consisting of 30 moderators from eight different countries.

MASS SPECTROMETRY: THE STATE OF PLAY IN THE UK

WRITTEN BY JAMES HAWLEY, JO ADAWAY AND BRIAN KEEVIL

Often considered a magic bullet for analytical measurements, liquid chromatography tandem mass spectrometry (or simply LC-MS/MS) has revolutionised clinical chemistry departments up and down the country. Since its earliest application for monitoring immunosuppressant drug concentrations in transplant patients, LC-MS/MS has expanded to provide services for many clinical disciplines, with large, multi-analyte profiles now available.

Here, we provide a brief introduction to the key stages in LC-MS/MS, before discussing the state of play in the UK for selected endocrine assays, including those for oestradiol, 5-hydroxyindoleacetic acid (5HIAA), metanephrines, cortisol and dexamethasone. Finally, we look at what the future holds.

Overall, SIMBA has proved to be an effective example of simulation-based learning in medical education for both medical trainees and students. Medical trainees' confidence in interpreting and managing clinical scenarios has significantly improved, whilst medical students feel more confident in both their clinical knowledge and professional self-development. These aspects are all transferable to future medical practice in providing optimal patient care.

You can find out more about SIMBA at <https://sites.google.com/view/simbasimulation>.

ANISAH ALI

3rd Year Medical Student, University of Birmingham Medical School

DENGYI ZHOU

4th Year Medical Student, University of Birmingham Medical School

PUNITH KEMPEGOWDA

Honorary Specialist Training Registrar in Endocrinology, Diabetes and General Internal Medicine, University Hospitals Birmingham NHS Foundation Trust, and Wellcome Trust Clinical Research Fellow, Institute of Metabolism and Systems Research, University of Birmingham

on behalf of the SIMBA team

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WHAT EXACTLY IS LC-MS/MS?

Broadly, the process of generating LC-MS/MS results can be thought of as three distinct processes, all of which must be given the appropriate attention to produce meaningful, accurate results.

The first of these is sample preparation. The choice here is dependent on several factors, including the concentration of the target analyte (nmol/l versus pmol/l), sample matrix (serum, urine, saliva), turnaround time, the chemical properties of the analyte and, last but not least, the cost of the consumables. In general, the more challenging the analyte is to measure, the greater the sample volume and the more intensive the sample clean-up required.

Next, we turn our attention to liquid chromatography. This helps separate the analyte of interest from other compounds, based on the analyte's physicochemical properties. It is paramount to ensure that the analyte of interest is separated from potential interferents and is not compromised by matrix effects, which can be the Achilles' heel of many methods. Whereas matrix effects can be difficult to predict, attention to detail can go some way to ensure your target analyte is not interfered with by another compound.

It is practically impossible to distinguish isobaric compounds (i.e. those of the same molecular weight) from one another using only mass spectrometry. This is especially true of steroid hormones, where the masses are commonly the same as neighbouring precursors or metabolites. In these situations, chromatography really comes into its own, and is an essential component of developing specific methods.

The final stage, of course, involves the mass spectrometer itself. Although it is simply a detector, it is a very sensitive one. Being reliant on mass-to-charge, it holds a distinct advantage over other approaches (e.g. assays reliant on antibody-antigen reactions). Furthermore, with tandem mass spectrometry, you have the ability to fragment the analyte of interest to look for products of your target analyte. This adds another layer of assurance that what you are detecting is what you believe it to be.

When these processes are combined, you can develop robust and accurate assays that are clinically useful. There is a huge interest in LC-MS/MS within the UK, and clinical laboratories are increasingly active in assay development. In case you may have missed it, the following are some of the major applications that have become available.

OESTRADIOL

Sensitive oestradiol measurements may be required to help investigate precocious puberty, gynaecomastia, post-menopausal females and patients taking aromatase inhibitors. This measurement can prove particularly problematic for immunoassays as, with functional sensitivities of approximately 100pmol/l, they simply don't measure low enough to be informative. Taken in conjunction with their inherent poor specificity, when you do have a result, you can't be sure it's meaningful (e.g. interference within the immunoassay with fulvestrant¹). With LC-MS/MS assays that measure down to 3pmol/l now available in the UK, the diagnosis and monitoring of the aforementioned patient groups are now achievable.

5HIAA

Mass spectrometry assays have also been successfully used to help advance the investigation of neuroendocrine tumours. As concentrations are an order of magnitude greater in urine than in serum, traditionally only 24-h urine collection could be used to quantify 5HIAA. However, following the development of more sensitive LC-MS/MS instrumentation, several assays for serum and plasma 5HIAA are now available in the UK. These offer more convenience for patients, are less susceptible to dietary influences, and are not prone to under- or over-collection of urine.²

METANEPHRINES

Screening for pheochromocytoma has also benefited from moving from urine to plasma in recent years. This has largely been facilitated by the development of LC-MS/MS assays. Some centres also offer 3-methoxytyramine as standard to help identify dopamine-secreting tumours, as well as head and neck paragangliomas.³

CORTISOL

The questionable performance of some serum cortisol immunoassay measurements is well reported.⁴ Both the poor specificity of antibodies and the inability of some assays to liberate cortisol from its binding globulin have established a requirement for accurate measurements. This is especially true for patients on existing glucocorticoid regimens or those taking metyrapone to treat Cushing's syndrome.

These problems have successfully been circumnavigated using LC-MS/MS, and several services are now available within the UK. With the provision of mass spectrometry, a new debate is emerging with regard to how urgently cortisol results should be provided. Is there a need for an accurate result in <24h, or is it imperative to provide a result that may or may not be close

to the true value in under an hour (or a little over)? (Please note: if you feel particularly strongly about this, I would welcome your informed opinion!)

DEXAMETHASONE

In a similar way, although cortisol immunoassays tend not to suffer from dexamethasone interference, some patients may not adhere to the 1mg overnight dexamethasone protocol and others may have *CYP3A4* mutations that mean they will quickly metabolise the drug. As serum LC-MS/MS dexamethasone assays are now routinely available, it is possible to identify false-positive results before going on to arrange imaging.⁵

'There is a huge interest in LC-MS/MS within the UK, and clinical laboratories are increasingly active in assay development.'

THE FUTURE

As we move into the next decade, there are several exciting developments in endocrinology that promise to be further elucidated using mass spectrometry. Considerable research is being undertaken to look at 11-oxoandrogens in polycystic ovary syndrome, congenital adrenal hyperplasia and precocious puberty. With serum and saliva assays available,^{6,7} there promises to be further input from UK-based laboratories in this emerging field. Indeed, with salivary testing still in its infancy, growing evidence suggests that the use of salivary cortisone may more accurately correlate with serum free cortisol concentrations. This is finding new applications in the diagnosis and monitoring of adrenal disorders.⁸

The promise of complementing mass spectrometry with data science has been realised by the Arlt group in Birmingham, as they have shown that LC-MS/MS urine steroid profiling can be used alongside machine learning to enhance the detection of adrenocortical carcinomas.⁹ This revolutionary approach could be applied to other conditions that rely on LC-MS/MS profiling rather than absolute quantification of a target analyte.

Finally, the use of LC-MS/MS to quantify protein markers has been under-utilised in UK laboratories. As methods for insulin¹⁰ and thyroglobulin¹¹ have been published, it is likely that this deficiency will be addressed sooner rather than later.

If you are interested in knowing more about the assays discussed above, or mass spectrometry in general, please feel free to contact me at james.hawley@mft.nhs.uk.

JAMES HAWLEY, JO ADAWAY AND BRIAN KEEVIL

Wythenshawe Hospital, Manchester University NHS Foundation Trust

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IT'S TIME TO JOIN THE EARS COMMUNITY!

WRITTEN BY MARTIN REINCKE AND ANTON LUGER



The new European Society of Endocrinology (ESE) Advocacy Representation Scheme (EARS) launched in October, following careful consultation with ESE Council of Affiliated Societies (ECAS) representatives. EARS enables ESE's National Affiliated Societies and their members to engage with its policy and advocacy work, so ensuring endocrinologists' voices are heard across Europe.

WHY ARE POLICY AND ADVOCACY SO IMPORTANT?

ESE's mission statement, 'Shaping the Future of Endocrinology', requires it to interact with stakeholders, so that the importance of endocrine health is recognised when healthcare policies and research programme support are developed.

WHY SHOULD YOU JOIN THE EARS COMMUNITY?

The main reason for you to get involved is that endocrinologists are stronger together. ESE is the VOICE for ENDOCRINOLOGY in Brussels. The EARS scheme means ESE will represent a community of over 22,500 endocrine healthcare professionals and researchers across Europe, as well as the patients they care for. This community cannot remain unheard!

WHAT DOES JOINING EARS MEAN?

You will:

- receive regular e-newsletter updates on ESE's policy and advocacy work
- be consulted on policy and advocacy activities
- have your voice heard as part of Europe's endocrinology community
- be able to access resources, such as the ESE White Paper (see panel)
- be invited to relevant events, e.g. during the European Congress of Endocrinology (ECE) and on topics such as research funding.

Joining is FREE for members of ESE's National Affiliated Societies (represented by ECAS) and – as the Society for Endocrinology has already paid the small fee of €2.50 on your behalf – all you need to do, to receive the benefits above, is to join the EARS Community at <https://bit.ly/JoinEARS>.

WHAT DOES ESE'S POLICY AND ADVOCACY WORK INCLUDE?

It focuses on three areas of strategic importance to the European and global healthcare agenda:

- achieving greater healthcare effectiveness and resilience through health promotion and disease prevention, particularly post-COVID-19 recovery, and its impact regarding endocrine and metabolic diseases
- supporting the 'Mission on Cancer', contributing to the 'Beating Cancer Plan' and stimulating research on endocrine origins and consequences
- engaging in EU debates on climate change and the environment, particularly endocrine disruptors.

WHAT HAS ESE ACHIEVED SO FAR?

Over the last 12 months, ESE has focused on inserting the hormone health perspective into the **Horizon Europe** research programme, the **Beating Cancer Plan**, support to rare diseases within the **European Reference Networks** and, more recently (driven by the impact of the COVID-19 pandemic), the **EU4Health Programme**. The Commission's **Green Deal** and, as part of that, the **Chemical Strategy for Sustainability** need to include a strong emphasis on endocrine disruptors, which are a major contributor to susceptibility to many non-communicable diseases. To read more, visit www.eese-hormones.org/advocacy.

We look forward to welcoming you into the EARS Community. Join EARS today: sign up at <https://bit.ly/JoinEARS>.

MARTIN REINCKE
ESE President-Elect

ANTON LUGER
ECAS Representative

ESE'S NEW WHITE PAPER TO PROMOTE ENDOCRINOLOGY!

Early 2021 sees the launch of ESE's White Paper on endocrinology. Its main aim is to explain and highlight to EU policymakers the importance of endocrinology as a discipline.

The White Paper, entitled 'Hormones in European health policies: contributing towards a healthier Europe', encourages the EU to bring endocrinology to the forefront of upcoming policies on health, such as the Beating Cancer Plan and the EU4Health Programme. The development of the White Paper has been led by the ESE Policy and Advocacy Task Force, which contributed extensively to it during the whole drafting process.

It focuses on four priority areas: rare diseases, obesity, cancer and endocrine-disrupting chemicals (EDCs). These were chosen because of their relevance to the field of endocrinology as well as current policy focus.

Readers are first provided with an overview of what endocrinology is, and the functions controlled by hormones and their importance. The White Paper uses data from ESE's 2018 Mapping Endocrinology in Europe (MEnEu) survey to show where endocrinologists specialise, as well as the field's multidisciplinary nature.

Each chapter (rare diseases, obesity, cancer and EDCs) describes the links between that area and endocrinology, and gives an overview of the main related EU policies. The chapters aim to identify what the EU is doing well and what could be improved, from the perspective of endocrinology. Where relevant, the chapters also contextualise the impact of COVID-19.

Finally, the White Paper gives a set of concrete expert policy recommendations addressed to EU policymakers in each of the areas.

The White Paper has been through a comprehensive developmental process lasting several years. Drafting it combined desk-based research with quantitative input from the MEnEu survey and qualitative input from interviews with ESE experts and patients. It was submitted for consultation and review to experts of the ESE Policy and Advocacy Task Force and ESE Executive Committee. It was also reviewed and endorsed by the 54 national societies represented through the ESE Council of Affiliated Societies (ECAS).

You will soon be able to read the White Paper at www.eese-hormones.org/advocacy. Join a specific session on this, and the breadth of ESE's policy and advocacy work, at e-ECE 2021 on 22–26 May 2021. Find out more at www.ece2021.org.

2021 is our 75th anniversary!

CELEBRATE YOUR SOCIETY'S BIRTHDAY



We have all been through some exceptionally challenging times over the last year, making it all the more important to wholeheartedly mark this anniversary of our Society, the home of endocrinology for 75 years.

Let's seize this opportunity to celebrate our discipline and the work of endocrinologists, revel in our achievements together, and look forward to the flourishing future of endocrinology. Whether you are a Society rookie or a veteran, a student or a seasoned professional, we want to hear from you!

Our members make the Society. Your hard work, stories and aspirations have all contributed to our phenomenal journey over the last 75 years, and will form the foundations of our future successes. Get involved with the upcoming festivities by sharing your memories, thoughts, photos and achievements.

- Do you have any photos from Society events to share?
- Who is your most inspirational endocrinologist and why?
- When did you attend your first SfE BES conference and what did you enjoy most?
- What are your favourite memories of working with the Society and other members?
- How has being a Society member benefited your career?
- How much has the Society changed since you joined?
- What are you most looking forward to as part of the Society's future and the field of endocrinology?

Send us a line or two in answer to the above – or about anything else you would like to share. Your contributions will be used as part of our year-long celebrations, to truly reflect the value of being part of the Society for Endocrinology.

Watch out for more 75th anniversary activities coming very soon!

Send your contributions, suggestions or queries to **media@endocrinology.org** by **15 May 2021**.

Celebrating excellence in endocrinology

OUR 2021 MEDALLISTS AND AWARDEES

After a challenging 2020, join us in sharing some positivity by congratulating our 2021 medallists and awardees!

These world-leading endocrinologists have made significant contributions to advancing research, knowledge and clinical practice in our field. Our medallists will present plenary lectures at the Society for Endocrinology BES conference on 8-11 November 2021.



DALE MEDAL
Sadaf Farooqi
Cambridge, UK



INTERNATIONAL MEDAL
Mark Febbraio
Monash, Victoria, Australia

“The Society is a wonderful organisation, committed to advancing scientific and clinical education and research in endocrinology for the public benefit. To be selected as the winner of the International Medal is a great honour. To see my name in the company of so many outstanding previous winners is humbling. I look forward to participating in SfE BES 2021.



EUROPEAN MEDAL
Greet Van den Berghe
Leuven, Belgium

“Receiving the European Medal came as a total surprise! It is a great encouragement for me and an honour, especially given my somewhat atypical background in intensive care medicine and my focus on endocrinology and critical illness. Looking at the names of previous eminent awardees of the European Medal, I never thought I'd be among them! It's really awesome!

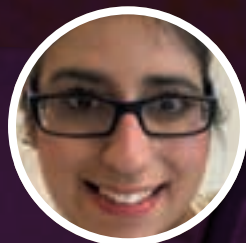


JUBILEE MEDAL
Stephen Shalet
Manchester, UK

“I am thrilled to be the Jubilee Medallist for 2021. I joined the Society at the very start of my career when I was just starting out in my specialty, so I feel a special attachment.

Last year we launched our new Teaching Achievement and Outstanding Clinical Practitioner Awards, to recognise excellence in teaching and in delivering patient care. We are delighted to present them for the first time in 2021.

TEACHING ACHIEVEMENT AWARD



Sheba Jarvis
London, UK

“Thank you to the Society for this award. I feel humbled to have been nominated in the first place, so to receive the award is a true privilege! Teaching allows me to learn more about myself and it is a complete joy. I am grateful to the people at Imperial (and other mentors beyond) who have supported and helped harness my enthusiasm.



Niamh Martin
London, UK

“I am delighted that the Society has initiated this new award to recognise the teaching which helps to shape our endocrinologists of the future, and I am very grateful to receive it.



NIKKI KIEFFER MEDAL

Anne Marland
Oxford, UK



STARLING MEDAL

Roland Stimson
Edinburgh, UK

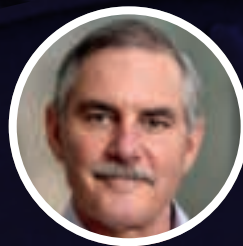
“ I’m deeply honoured to receive the Starling Medal. To be nominated is very humbling, particularly when you see the past recipients and the fantastic work they’ve performed. I very much look forward to presenting our research next year, and it will be great to see everyone in person in Edinburgh.



SOCIETY MEDAL

Jeremy Tomlinson
Oxford, UK

“ I am absolutely delighted to win this medal. It was a complete surprise and I feel very honoured to be nominated by my colleagues and peers – amazing! Over the years, I have had the privilege of working with some really talented individuals and our research has always been a collaborative, team endeavour, so this really does reflect their hard work and success, as much as mine.



TRANSATLANTIC MEDAL

David D Moore
Houston, TX, USA

“ Particularly in these very difficult times, I deeply appreciate the award of the Transatlantic Medal from the Society. It is a tremendous honour to join the distinguished list of recipients and I am very much looking forward to being in Edinburgh in November 2021.

OUTSTANDING CLINICAL PRACTITIONER AWARD



Kristien Boelaert
Birmingham, UK

“ I am delighted to be the recipient of this award, and I feel honoured to share it with Helen Simpson, who has done such amazing work on the new steroid card for patients. This award is a culmination of the outstanding clinical and research teams of colleagues, mentors and trainees I have been fortunate to work with over the years. Special thanks also go to the patient support groups, the funding bodies, the professional societies and my family, who have been instrumental in shaping my career.



Helen Simpson
London, UK

“ I’m honoured to be the recipient of this award, and I am equally honoured to share it with Kristien Boelaert, who works tirelessly to support patients with thyroid disorders. It is great to see the Society recognising clinical practice. A smiling patient never fails to bring a smile to my own face. Thanks to my colleagues and the Society for support over the years, to my patients and the patient support groups, and extra special gratefulness goes to my teenager. I look forward to celebrating with my award twin and everyone else, hopefully, in Edinburgh in 2021.

Your evolving Society: WORKING TO MEET OUR MEMBERS' NEEDS

FIT FOR THE FUTURE: A HEALTH CHECK FOR YOUR SOCIETY

As the Society celebrates its 75th anniversary, it's astonishing to think how much the field of endocrinology has developed in that time and how diverse our community is across the scientific-clinical spectrum. It's a tough job for a Society to cater for so many different and constantly evolving needs.



Last year, I was appointed by Council to chair a working group to conduct a review of the Society's governance, including the structure of our Council and Committees and other groups, the breadth of expertise within them, and the processes that underpin them. It is equally important to consider how transparent that governance is to the membership. Ultimately, the purpose of this review is to ensure that the Society is fit for purpose now and well into the future.

It's important to say that this review has not come about because of any complaints or instructions to do so, but simply because we know it is best practice to regularly review these things. With the increasing importance of diversity and inclusion within organisations (even more so for a field as broad as endocrinology!), it felt timely to review our governance as a whole.

In October 2020, we put out an open call to the membership in order to recruit a group of members to oversee the review process. Our group is being supported and guided by an external consultant who specialises in governance for learned societies and charities. She is ensuring we approach the review objectively, based on sound governance principles.

Broadly, the working group will review the Society's governance against all aspects of the Charity Governance Code, namely:

- leadership
- integrity
- decision making, risk and control
- board effectiveness
- equality diversity and inclusion, and
- openness and accountability.

Aside from a few technical matters, good governance is mostly about upholding common sense, integrity and fairness. Some of the specific areas we have started to consider are our processes for appointing key roles within the Society (e.g. Officers or Committee

Chairs), the data we capture about our members to enable us to better monitor diversity and inclusion, whether our Endocrine Networks should be a more formal part of our governance structure, and how we can encourage more diversity on our Committees.

We are busy gathering member feedback on all aspects of governance through a series of individual interviews, focus groups and surveys. All of this will be considered, alongside examples of good practice in other organisations, to help us draft a series of recommendations for change. We will be inviting all members to feed back their views on these recommendations before they are presented to Council.

In the meantime, if you have any particular areas that you feel should be addressed by the working group, please let us know at Karen.Chapman@ed.ac.uk or members@endocrinology.org, and we will make sure your points are considered.

The end result of this process will be an even more robust, representative and transparent Society that can continue meeting its members' evolving needs well into the future!

GOVERNANCE REVIEW WORKING GROUP MEMBERS

KAREN CHAPMAN
Chair, Scientist, Edinburgh

TIM COLE
Scientist, Melbourne, Australia

HILARY CRITCHLEY
Clinical Academic, Edinburgh

CHONA FELICIANO
Nurse, Birmingham

ANNEKE GRAF
Early Career Clinician, London

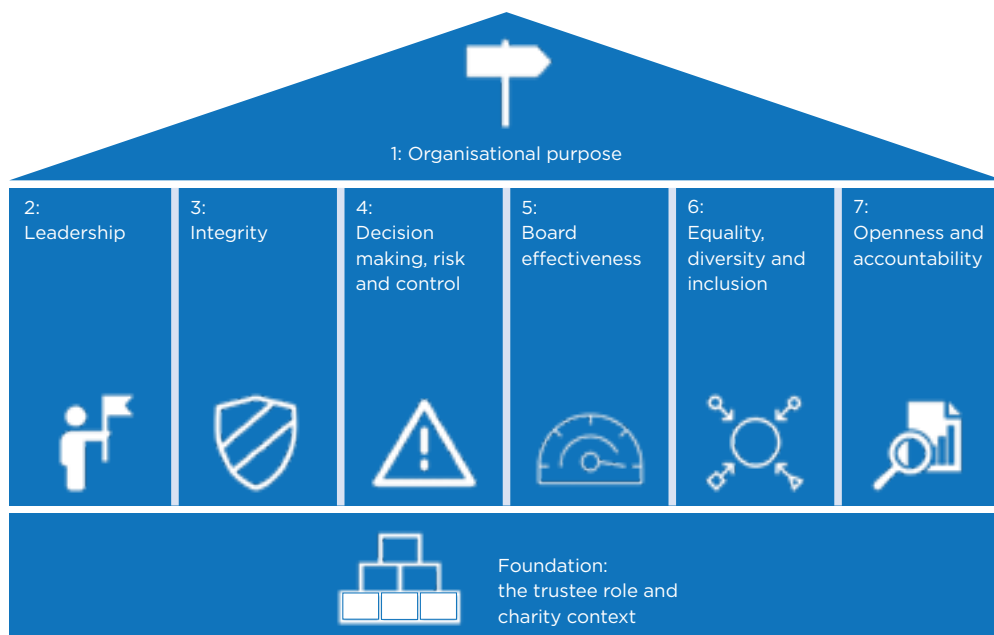
STEVE ORME
Clinician, Leeds

JESSICA PIASECKI
Early Career Scientist, Nottingham

DOUG ROBERTSON
Clinician, Cheshire

CLAIRE STEWART
Scientist, Liverpool

JEREMY TOMLINSON
Clinical Academic, Oxford



KAREN CHAPMAN

A HELPING HAND TO SHARE GOOD CLINICAL PRACTICE

While the ongoing pandemic has massively disrupted endocrine service provision, it has also lent us the opportunity to consider how services might be configured if we were to start 'afresh' and design anew.

Last year, our Future of Endocrinology working group was set up, co-chaired by John Newell-Price (Sheffield) and Kristien Boelaert (Birmingham). The remit is wide-ranging, with multiple partners, and includes attention to innovative models of care, remote working, patient pathways, teaching and training, research and innovation, and sharing of best practice. One area, 'Response to COVID-19', has already been completed and is live on the Society's website (see panel on right).

One of the outputs from this group will be the creation of a new Society-managed resource bank that will allow members to share examples of protocols, template letters, information sheets, care models – and more – with other Society members. We hope that this will reduce the current amount of 'reinventing the wheel' necessary for each Trust, and allow members to effectively learn from what other clinician or nurse members have already put into practice.

If you have suggestions for useful content where you feel there is a gap or, alternatively, helpful resources that you'd be willing to share in this way, please let us know at clinical@endocrinology.org.

COVID-19 RESOURCES

Our COVID-19 resources for managing endocrine conditions, and recommendations for continuing endocrine services through the pandemic, are all available now at www.endocrinology.org/covid19.

STREAMLINING NHS SERVICES WITH SPECIALISED ENDOCRINOLOGY NETWORKS

During a number of my Getting It Right First Time (GIRFT) visits, my colleagues and I discussed the management and experience of rarer cases in endocrinology and, more specifically, the importance of having readily available expertise.

Clearly, experience of looking after rarer cases (for example, of hypoparathyroidism) is essential. So, we developed the idea of having a number of special interest networks across the country under the aegis of the Society for Endocrinology. The Specialised Endocrinology Clinical Reference Group is also looking at this network format to develop more coherent NHS services.

In the last couple of months, we have gone a significant way in setting up groups with special interests in:

- bone and mineral endocrinology (led by Jeremy Turner and Neil Gittoes)
- andrology (led by Channa Jayasena)
- transgender medicine (led by Leighton Seal).

Our aim is to bring together groups of clinicians in similar geographical locations, who are especially interested in these conditions.

The purpose of these networks would be to ensure the provision of experience in some of these rarer forms of endocrinology, within each locality. In addition to improving the management of patients, networks would be a great source of teaching resources for our trainees and colleagues. The combined strength within each network could

also be used to set up and run research programmes in these subspecialties. We envisage that these groups will meet two to three times a year (virtually at first).

The Society for Endocrinology's Clinical Committee have approved and support this invaluable initiative. You will soon receive invitations from the Society to apply to join these groups. I strongly encourage you to do so; this is an important scheme for the advancement and standardisation of specialised patient care.

If you have any queries, please contact us at clinical@endocrinology.org.

JOHN WASS
GIRFT

in association with:

JOHN NEWELL-PRICE
Specialised Endocrinology CRG,
Society's Future of Endocrinology working group

NEIL GITTOES
Specialised Endocrinology CRG,
Bone and Mineral Co-Lead

JEREMY TURNER
Bone and Mineral Co-Lead

CHANNA JAYASENA
Andrology Lead

LEIGHTON SEAL
Transgender Medicine Lead

ZOE PLUMMER
Society for Endocrinology



PERSPECTIVES OF SUCCESSFUL WOMEN

DISCUSSED BY KERRI DEVINE AND PHILIPPA SAUNDERS



FIRST PUBLISHED IN ISSUE 131 (SPRING 2019)

To mark International Women's Day 2021, which was on 8 March, we are revisiting this fascinating conversation from the archives. Early career clinician scientist Kerri Devine and senior academic Philippa Saunders discuss the challenges of networking, peer support, balancing family and budgeting time.

P: How has your career developed so far?

K: After undergraduate medicine with an intercalated BSc, 7 years of clinical training, including 2 years as a diabetes and endocrinology registrar, I've just become a student again and started my PhD.

P: How did you manage to get taken on to do a PhD, because that's quite a big step isn't it?

K: It is a big step and I think, perhaps especially for women, that timing is everything. I came to Newcastle for my specialty training and knew I wanted this to include some time in research. I initially approached Simon Pearce (my co-supervisor on my PhD) who introduced me to Brian Walker. He had recently come to Newcastle and was actively looking for someone to join him on an existing project. So I was looking and they were looking for me, and we matched!

P: Did your local NHS Postgraduate Dean have to give permission for you to take time out?

K: Yes, that is essential. I sit on the regional Specialty Training Committee and I'm also on the Early Career Steering Group for the Society for Endocrinology. Because of recent issues with trainee recruitment, trainees entering research is an area that could be compromised. I know the Deanery are really passionate about trainees still going into research, but it is a concern and such a key aspect of the specialty.

P: This highlights the importance, I believe, of leadership within our universities. By that, I mean it is important that senior academics both encourage and support clinical research trainees. One of my biggest tips for making the most of this training opportunity is to think ahead to your exit strategy. It is good to make sure that you draw not only on the support of your supervisors but also on that of a peer group. Some of the best support I've had in keeping going as a woman in science has come from peers.

K: I'm fortunate to work alongside female clinical academics who have now come out of training and who have been very supportive and very encouraging. Some of them are also mothers now, and they give advice on how to maintain balance and demonstrate that it is possible. I think that is so helpful and inspiring.

P: Yes, the team around you can be vital. So what have you done so far in your PhD?

K: My project is on tissue-specific differences in steroid metabolism, focusing on the ABC (ATP-binding cassette) transporter family. I'm following on from work by Catriona Kyle, who was a winning presenter at the Society for Endocrinology BES conference. At the moment, I'm going through the process of procurement and sponsorship for a clinical study. It's a big change for me. I've gone from having every

moment of my day accounted for and planned by someone else, to having to plan everything for myself.

P: That's a very honest appraisal of the real differences between feeling each day is full and that you can make a difference to people, and moving to the self-directed aspect of PhD work. Keep in mind why you're doing it and what you want to get out of it, because that can be really helpful in keeping up momentum and remaining positive when things are going slowly. Are you going to do any work with patients or is it all very much a science project?

K: No, a large part of my work will be on healthy volunteers, but it's a pathway to providing new solutions for patients that could make a big difference. Congenital adrenal hyperplasia (CAH) is an intended target patient group, so I'm making links with the teams in Newcastle who are looking after patients with CAH, and hope to continue this relationship after the PhD.

P: Building all those links is great, and will be invaluable in making the transition to the next stage of your career. I think it's very important not to be shy about going to meetings and making sure you take every opportunity to present your work.

K: Something I've heard discussed recently is that women can appear less inclined to respond to calls to present their work – to call themselves experts on the topic – and to step forward. Is this something that you have found?

P: I think there is plenty of evidence that women can be reluctant to put themselves forward for senior or leadership roles. Personally, I would say it's not that we don't have confidence in our own expertise, but I know I have felt anxious that if I am not successful it will in some way reflect badly on me and I will be labelled as being 'pushy'.

K: I've found it so helpful if someone who has 'been there before' supports you to put yourself forward. It does give you that extra self-belief.

P: Absolutely!

K: Earlier, you mentioned maintaining momentum. I think this is something that naturally puts women at a disadvantage. The stage

'It's all about building structures and networks so that you've got a support system ... That would be my top tip – draw down on every bit of support you can get.'

'I am pleased to say that things are improving rapidly, which is good, as it used to be unbelievably sexist... Sometimes being a bit tough can pay off!'

at which you might start to publish, and to develop some form of reputation in the field, is also the time when you are reaching the point of having a family. How do you juggle that?

P: There's no right or wrong time. Children don't come to order. You mustn't short-change yourself by cutting maternity leave short because you think you're going to miss out at work.

Maintaining momentum is very much about putting things in place that can back you up. So, before going on maternity leave, make sure you have people who are going to communicate with you, maybe get a small grant before you go off so you've got something to come back to. It's all about building structures and networks so that you've got a support system.

That would be my top tip – draw down on every bit of support you can get.

K: In your position, you must be called upon to do so much. Do you ever feel like you can say no?

P: You have to learn to say no. When you're trying to establish your career, you're tempted to say yes to everybody and everything, but this can make you tired and resentful. Also, if there are fewer senior women in the department, they tend to get asked to do more.

I am pleased to say that things are improving rapidly, which is good, as it used to be unbelievably sexist. I was once asked to be part of a funding application by the head of the department as they needed 'a non-clinical woman' on the group. It wasn't anything to do with my skills or talents, it was just to 'tick a box'! After we got the money I felt bolder; I told them they had to give me a personal Chair and they did so. Sometimes being a bit tough can pay off!

K: Do you think attitudes have changed to women in academia as you've moved through your career?

P: I think attitudes are improving.

K: You mentioned that at the Academy of Medical Sciences you do lots of things to try and encourage women into those prestigious senior positions?

P: We're really trying to encourage people to get nominated. We insist that every committee is gender-balanced, and that everyone has to be trained in unconscious bias.

It's difficult to hit our target of 35% of elected fellows being women, but it's much better with grants and other schemes. Certainly on the grant panel I run – which is called 'Springboard' – the split among successful grant recipients is 50:50 between men and women. The Academy has some particular schemes that support women: one called Inspire is aimed at medical students, and the other, for lecturers, is called Sustain.

In terms of the fellowship, the Academy started 20 years ago, and there was a founding fellows pool where people were invited to be fellows – only 7% of those were women! Our target is 35% women to be elected each year. We're currently at about 33%, so there is still some way to go.

P: So, do you feel well supported in terms of whatever you might want to do?

K: Yes absolutely. My supervisors are very supportive and experienced in working with clinicians, with women in research and with managing career breaks. And, as you say, we do always have an eye on what is going to come next. Going back into clinical medicine is going to be a big challenge. I won't have been practising for a few years. It's going to be a learning curve, both in terms of getting back into practice and in trying to keep some research going at the same time. And that's exactly the kind of time I'd be thinking about starting a family.

P: I've seen that with so many people and I think, if you're aware of that, you can mitigate against it. But it is a hard thing to go back. The PhD is just a really special time.

K: What is it about it that's so special?

P: It's that freedom. It's your project. What an incredible privilege to be able to spend 3 years working on something you're interested in, with the aim of improving medical care.

K: The ultimate privilege, isn't it? I only hope I can get everything done on time!

P: Be organised, get yourself out on time. It's much easier because then you can apply for other things, otherwise you do lose momentum. I think that's important. Good luck!

KERRI DEVINE

Clinical Research Fellow, Diabetes and Endocrinology Trainee (OOPR), Specialty Training Committee, Newcastle University/Northern Deanery, and Society for Endocrinology Early Career Steering Group

PHILIPPA SAUNDERS

Registrar, Academy of Medical Sciences; Professor of Reproductive Steroids, University of Edinburgh Centre for Inflammation Research, Queen's Medical Research Institute, Edinburgh

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Let's make lack of awareness around rare diseases

EVEN RARER

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TOGETHER, we leave no patient behind

To contact HRA Pharma Rare Diseases in the UK & Ireland email med.info.uk@hra-pharma.com or call 0800 917 9548.